THE BRITISH JOURNAL OF

TUBERCULOSIS

AND

DISEASES OF THE CHEST

Editor

PHILIP ELLMAN

April 1955

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NOTICE TO CONTRIBUTORS

Please turn to the inside back cover of this *Journal* for
particulars regarding submission of articles to the Editor

A PRELIMINARY ENQUIRY INTO THE RELATIVE VALUE OF MINIATURE (70-mm.) FILMS AND LARGE FILMS IN THE RADIOLOGICAL DIAGNOSIS OF PULMONARY TUBERCULOSIS

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Introduction

THE original purpose of this investigation was to examine the extent to which 70-mm. X-ray films could be used to replace standard large films in the identification of minimal tuberculous lesions. As our discussions proceeded, our objects broadened in scope in order to take into account the variability which was likely to occur in the reading not only of miniature films but also of standard films. The aims of the enquiry became (i) to compare the efficiency of 70-mm. films with that of standard films in diagnosing tuberculosis of the lungs (efficiency both in detecting the maximum number of true cases and in diagnosing the minimum number of false cases); and (ii) to assess the intra-observer and inter-observer variability in film readings of the two types of film.

Details of procedure will be described hereafter. It was considered necessary to undertake a pilot enquiry based on the interpretation of 300 pairs (large and small) of films by three consultant chest physicians and a consultant radiologist. From the pilot study, estimates of variability associated with different factors could be obtained, and a further series of film pairs would then be interpreted if the numbers in the pilot study were not found adequate.

Observer " Error." In attempting to assess the relative efficiency of large and small films, it is necessary to take into account the accuracy of film reading and to estimate the variability which might be attributed to the individual readers of films or to the differences between readers. Moreover, it is necessary to make allowance for the inaccuracy in large film reading if small film reading is to be judged in relation to large film. Several investigations into the accuracy of radiological interpretation are now available.

The Detection of Lesions. The investigations more immediately relevant to

our enquiry were those of Birkelo *et al.* (1947), Groth-Petersen *et al.* (1952), Yerushalmy *et al.* (1950) and Yerushalmy (1953). From their work it appeared that (i) the proportion of genuine cases which might be identified by a single reader was from 68 per cent. to 75 per cent.; (ii) a reader was likely to change his mind on a second reading once in about five cases; and (iii) a second independent observer would detect about half the cases missed by the first reader, but at the cost of erroneously diagnosing an increased number of " false positives " among the genuinely normal cases.

As a result of their findings, our investigation was planned to take the 70-mm. and the standard X-ray at the *same* time; to incorporate *dual reading of small films* into the investigation from the beginning; to carry out *dual readings of large films* also; to decide on " true positives " at subsequent " truth sessions " of readers and radiologist jointly; and to ensure that the actual *number of " true positives "* in the series was *sufficiently large* to make conclusions valid.

The Classification of " Positive " Cases. Accuracy in diagnosis of " true positives " depends on what criterion of " positive for tuberculosis " is used. Newell *et al.* (1954) found that the agreement between readers varied considerably according to the classification used to describe lesions visible on the X-ray film. Agreement as to what was " active " and " inactive " was only 51 per cent. of truly active cases. This was nevertheless better than would be expected purely by chance, and therefore the term " active " had some discriminatory power, but it was not sufficiently useful. Cochrane and Garland (1952) also found that, when readers were asked to classify films according to whether tuberculosis was present or absent and, further, to decide, in those where tuberculosis was present, whether the lesion was active or inactive and, if inactive, whether it was clinically significant or not, the greatest variability was in the recording of activity. The least variability occurred in the division of lesions into " clinically significant " and " not clinically significant."

In the present enquiry we therefore adopted a classification based on that of Cochrane and Garland, but dividing lesions into " minimal " or " other stages " and subdividing minimal lesions into " soft " and " hard."

Present Investigation

The scope of the present investigation was planned so that ground not previously covered by other enquiries would be covered by us, difficulties met in the course of other enquiries could be to some extent overcome, and factors which might be associated with observer-variability could be assessed. The points of major importance elicited in previous work and the approach to these in the present enquiry are as follows:

Previous Investigations	*Present Investigation*
1. Difficulties in establishing " true positives " from small film.	(a) Large and small films taken of *all* cases at the same time
	(b) Subsequent " truth sessions."
2. No reference to " observer-error " on large film readings.	Dual readings of large films as well as of small films.
3. Differences in results according to classification used.	Combination of all types of classification.

Previous Investigations	*Present Investigation*
4. Small number of " truly positive " cases in normal mass survey.	" Salting " of series, to a level unknown to the readers.
5. Possible bias of readers who have expectation of low incidence of " true positives."	Batches of films sent to readers contained varying incidence—*no* " expectation."
6. Problem of assessing components of " observer-error " in different circumstances (*e.g.*, if incidence unusually high or low; or if fatigue or other factors intervene).	(*a*) Analysis of readings of different batches of films containing different levels of incidence.
	(*b*) Other factors recorded (*e.g.*, non-tuberculous respiratory disease, time of day, order of reading).

Procedure. The material for this investigation was collected from large and small films taken during the routine work of three chest centres. The cases were therefore not necessarily patients, nor even contacts of known patients, since two of the chest centres carry out screening of entrants to the Forces. The pairs of films were not seen by the three readers, but were forwarded directly to the co-ordinator, who made a final selection of 300 pairs. Using a code which enabled the number on each film to be changed for each circulation of films, and " shuffling " with other batches each time before circulating for the next reading, the co-ordinator ensured that no film or batch of films could be recognised and that the dual readings were completely independent. Each small film and each large film was read twice by each of the three readers —a total of twelve readings per patient—and each large film was also read by the co-ordinator.

Recording of Data. The radiological findings were recorded under the following headings:

1. No evidence of respiratory disorder.

2. Minimal tuberculosis:* (*a*) soft (and presumably active).

                    (*b*) hard but clinically significant.

                    (*c*) hard and not clinically significant.

                    (*d*) not classifiable under (*a*), (*b*) or (*c*) above.

3. Tuberculosis, other stages.†

4. Other respiratory conditions‡—these to be specified.

In recording these data the readers indicated the zone(s) of the lung(s) involved,

* *A Minimal Lesion* was defined as an opaque area not greater than 5 sq. cm. on a full-size plate, or a small cluster of discrete shadows whose aggregated area was estimated on inspection to be no greater than 5 sq. cm.

† *Tuberculosis, other stages* was held to be any lesion more than minimal, whether considered soft or hard. If two or more minimal lesions were seen in one lung, these were supposed to be aggregated and therefore called " other stages." In the first reading of small films, however, this practice was not consistently carried out, so that occasionally two minimal lesions were recorded in the same lung.

‡ *Other respiratory conditions* included not only genuine pathological states, but also artefacts and such anatomical variants as the reader considered worth noting. Hilar and pleural changes (occurring without parenchymal evidence of tuberculosis) were included in this category.

using the designations R.U. (right upper), L.L. (left lower), etc., as defined by the Ministry of Health Memorandum (1952). Readers were asked to follow, so far as possible, normal working conditions.

" *Truth Sessions.*" For final analysis it was necessary to arrive at an agreed verdict on each patient, and for this purpose the readers and co-ordinator met together to scrutinise each film on which there was any query. All readers in all readings had agreed that 88 pairs of films revealed no evidence of tuber-culosis, and these films were therefore not re-examined at the truth sessions. Of the remaining 212, there were 25 on which, even after much discussion, no agreement could be reached at the truth sessions. In rather similar circumstances Groth-Petersen *et al.* (1952) eliminated such cases from their investigation; but in the present enquiry the cases were followed up, and a later standard-size film and case notes were available for subsequent meetings. By these means an agreed verdict was reached on 20 of the 25 cases. The remaining 5 were finally excluded from the enquiry as being indeterminate. In this way the nearest approach to " truth " was determined, so that the previous interpretations of the 295 pairs of large and small films could be com-pared with the " truth."

Transfer to Punch-Cards. The items of information recorded in each reading were coded in detail to enable site, extent, stage and activity of lesions in each lung to be transferred to punch-cards; one card was used for each patient. It was thus possible to compare *strict* agreement of every detail of reading and classification by one reader with the detailed reading of the same or another reader on the same or different type of film. In interim analyses of first and second small-film readings this was actually done, and wide divergence between findings was revealed. As a result it was decided that for the initial purpose of the investigation—" efficiency " of film-reading—the most profitable basis of analysis would be to ignore details of discrepancies in readings and consider only the " result for the patient," *i.e.*, the action which would have been taken administratively on the basis of the radiological decision.

In the transfer of data to punch-cards, four categories of " result for the patient " were recorded; these were A=immediate action; F=follow-up after some interval; H=healed lesion; and N=no tuberculosis. These categories were maintained throughout the analyses and were then amalgamated in different ways in assessing the results; for example, " action " and " follow-up " cases were combined in one assessment, whilst " action," " follow-up " and " healed " cases were combined in another assessment, so that the estimated loss of genuine cases could be found when different administrative practices were postulated.

Results

GENERAL OBSERVATIONS BASED ON RESULTS OF TRUTH SESSIONS. As a result of the truth sessions described above, we agreed that 172 films showed no evidence of tuberculosis. These were designated " tuberculosis truly absent." Those showing some evidence of lesions, not necessarily significant, numbered 123. Quite apart from the question of " salting " the series, it should be emphasised that the ratio of true positives

to true negatives is much higher in clinic work dealing with referred cases and contacts than in mass surveys of a normal population.

Complete details of the decisions at the truth sessions were as follows:

Some Evidence of Tuberculosis—123.
Minimal lesions—Clinically not significant   ..   31 ⎫
               Hard but clinically significant   ..   15 ⎬ 83 ⎫ *
               Soft (presumed active)   ..   ..   37 ⎭   ⎬ 123
   Tuberculosis, other stages   ..   ..   40 ⎭

No Evidence of Tuberculosis—172.
Read " clear " on all twelve readings   ..   ..   88 ⎫
Read " tuberculosis " on some reading   ..   ..   84 ⎬   172
Total Cases   295

One other result of the truth sessions is worthy of note. In scrutinising the films we found 11 cases in which a small lesion was detected on the large film, but was not discernible on the small film even with careful examination and with knowledge of the site of the lesion. In one large film a similar concealment of a soft lesion occurred, though it was clearly visible on the small film. The concealment was found to occur in the site where the clavicle crossing the first rib casts a double bony shadow on the radiograph. The density of this small area may well be sufficient to hide a soft parenchymal lesion. It may be, therefore, that the position of the patient is all-important in producing a clear picture of certain minimal lesions, though the concealment may be less common in large than in small films. Such loss of " true positives," mostly soft lesions in upper zones, could be a serious matter in mass surveys. The problem may be solved if two films in different positions are taken, and we hope to investigate this possibility in a subsequent enquiry.

ANALYSIS OF VARIANCE. The technique of analysis of variance consists, briefly, of sequential comparisons of observations (either singly or in groups) with each other, and of estimates of variability associated with different factors in these comparisons. For example, inter-observer variability—whether a patient's film happened to be read by Dr. X or Dr. Y—can be separated from intra-observer variability—whether a patient seeing Dr. X happened to come one day or another—and both these factors can be separated from inter-film-type variability—whether a patient happened to come to clinic S which uses small film or to clinic L which uses large film. The analysis of variance is not concerned with the " true " reading for any film, but with the influence of different factors in contributing to variability of observations.

In this study the variance analysis was carried out algebraically, using the categories A, F, H and N previously defined, instead of by the more usual arithmetical method. The final algebraic estimates of variability were then translated into " result for the patient " according to different possible administrative procedures—for example, whether only A cases were at once followed up, or whether both A and F cases were regarded as requiring immediate follow-up. By this means it was possible to obtain numerical estimates of the total variability from all twelve readings and to subdivide this into (i) intra-observer variability within the four readings of one observer regardless of type of film, and inter-observer variability between the readings of different

* This number included 9 cases in which " tuberculosis, other stages " was present in addition to the minimal lesion recorded.

observers; (ii) intra-film variability within the six readings on one type of film regardless of reader, and inter-film-type variability between the group of small-film readings and the group of large-film readings; (iii) intra-observer and inter-observer variability within and between small-film and large-film dual readings; (iv) residual " unexplained " variability, not to be associated with dual reading, differences in readers or film-type.

Tables I to IV show the numerical estimates when the total variability was subdivided into components associated with these different factors. To the non-mathematical reader it should be pointed out that in this enquiry the index of variability could theoretically lie between zero (no variability) and unity (complete variability). In each table the five columns represent different amalgamations of A, F, H and N.

TABLE I.—ESTIMATES OF VARIANCE BETWEEN READERS' AVERAGE READINGS (INTER-OBSERVER AND WITHIN READERS' OWN FOUR READINGS (INTRA-OBSERVER)

Calculated for possible clinic practices in the recall of patients

	All four criteria considered simultaneously	Three criteria considered simultaneously	Criterion: tuberculosis present	Criterion: tuberculosis clinically significant	Criterion: tuberculosis active
	A, F, H, N all considered different	A=F; and H and N considered different	A=F=H; N different	A=F; and H=N (but A different from H)	A different F=H=N
	(1)	(2)	(3)	(4)	(5)
Between readers	·5303	·3341	·2649	·2374	·3530
Within readers' four readings	·3459	·2576	·2112	·1931	·2081
Within readers' four readings:					
Within duplicate readings ...	·2579	·1910	·1525	·1423	·1494
Between duplicate readings ...	·5220	·3907	·3286	·2948	·3255

Note: In each of Tables I, II, III, IV *the five columns* show the variance components according to different amalgamations of A, F, H and N.

(1) Column 1 shows the variance components if each of the diagnoses " active " (A), " significant " (F), " hard " (H), and " no lesion " (N) is treated as giving a different result for the patient.

(2) Column 2 shows the variance components if diagnoses of A and F are treated as giving the same result, but diagnoses of H or N are treated as giving different results for the patient.

(3) In Column 3, diagnoses indicating *any* evidence of tuberculosis (including apparently healed lesions) are treated as giving the same result for the patient.

(4) In Column 4, diagnoses of active or clinically significant lesions are treated as giving one result, whilst a diagnosis of a healed lesion is treated as giving the same result as " no lesion."

(5) In Column 5, a diagnosis of " active lesion " is treated as giving one result for the patient, whilst diagnoses of inactive or healed lesions or of no lesion are all treated as giving the same result.

It will be seen, firstly, that the average variability within a reader's own four readings was significantly less than variability between the three readers (Table I, first and second rows; ratio of first to second row gives the comparison). Thus there was greater self-consistency in the readings of any one observer—even though he was reading different-sized films—than there was between the readings of different observers. (This was found to be so, even when the different observers were reading the same-sized film.) The high inter-observer variability relative to intra-observer variability was most marked in the diagnosis

of active lesions (column 5). In diagnosing clinically significant lesions, the within-reader variability was only a little lower than the between-readers variability (column 4). It will be seen also that the intra-observer variability within duplicate readings (*i.e.*, on the same-sized film) was relatively small.

Secondly, Table II shows that, within readings on the same-sized film, variability was significantly lower than the variability between the two film-types. It is interesting to note that within the six large-film readings the variability was only slightly lower than within the six small-film readings; in fact, in diagnosing active lesions the variability within large-film readings was very slightly higher (column 5). Thus, if the six readings were treated as if made by six different observers, the consistency within large-film readings was only a little better than within small-film, except in diagnosing activity of lesions.

TABLE II.—ESTIMATES OF VARIANCE BETWEEN FILM-TYPES' AVERAGES AND
WITHIN FILM-TYPES

Calculated for possible clinic practices in the recall of patients

	A, F, H, N all all considered different	$A=F$; and H and N considered different	$A=F=H$; N different	$A=F$; and $H=N$; (but A different from H)	A different; $F=H=N$
	(1)	(2)	(3)	(4)	(5)
Between film-averages ..	·7115	·6297	·5220	·4976	·4088
Within film-types ..	·3462	·2357	·1909	·1715	·2170
Within film-types: Within six small-film readings ..	·3616	·2594	·2107	·1899	·2129
Within six large-film readings ..	·3308	·2119	·1711	·1531	·2211

However, the six readings were *not* made by six observers but by three, and the within-film variability was due partly to divergencies occurring within the duplicate readings of the three and partly to divergencies between the three observers. When these components were separated (Table III), it was found that an observer's self-consistency in dual reading was slightly better on large films than on small. On the other hand, consistency *between* different observers was on the whole slightly worse when reading large films than small.

The lowest line of Table III shows also that the variability between the average of the small-film and the average of the large-film readings was significantly greater than either intra-observer or inter-observer variability. It must be remembered, however, that discussions during the course of the small-film readings gave rise to some changes in recording, and these resulted in some discrepancies between first and second small-film readings. Moreover, as already mentioned, there were some small films on which lesions were not discernible, and these accounted for a considerable part of the inter-film-type variability. It is interesting to note that variability between film-types was least in the diagnosis of activity (column 5).

Finally, Table IV summarises the measures of variability which may be

associated with the four main factors—viz., divergencies between dual readings (replication), divergencies between readers (inter-observer), divergencies between films (inter-film-type), and residual variability unaccounted for by these factors. It can be seen that the unexplained residual variability was comparatively small in the diagnosis of clinically significant lesions (column 4), but rose sharply in the diagnosis of activity.

TABLE III.—ESTIMATES OF VARIANCE WITHIN READERS AND BETWEEN READERS AND WITHIN FILMS AND BETWEEN FILMS, SHOWING COMPONENTS ASSOCIATED WITH DUPLICATE READING (REPLICATION)

Calculated for possible clinic practices in the recall of patients

	A, F, H, N all considered different	A=F; and H and N considered different	A=F=H; N different	A=F; and H=N; (but A different from H)	A different; F=H=N
	(1)	(2)	(3)	(4)	(5)
Intra-observer:					
Within small-film paired readings ..	·2925	·2296	·1824	·1730	·1557
Within large-film paired readings ..	·2233	·1525	·1226	·1116	·1431
Inter-Observer:					
Between small-film paired readings ..	·4654	·3042	·2531	·2154	·2987
Between large-film paired readings ..	·4921	·3011	·2437	·2154	·3381
Inter-film type:					
Between film averages ..	·7115	·6297	·5220	·4976	·4088

TABLE IV.—SUMMARY OF VARIANCE—ESTIMATES ASSOCIATED WITH DIFFERENT FACTORS

Calculated for possible clinic practices in the recall of patients

	A, F, H, N all considered different	A=F; and H and N considered different	A=F=H; N different	A=F; and H=N; (but A different from H)	A different; F=H=N
	(1)	(2)	(3)	(4)	(5)
Replication— effect ..	·2579	·1910	·1525	·1423	·1494
Reader— effect ..	·5303	·3341	·2649	·2374	·3530
Film— effect ..	·7115	·6297	·5220	·4976	·4088
Residual (un-explained)..	·4273	·2712	·2319	·1934	·2838

Thus Tables I to IV show that the magnitude of " reader effect " was considerable, though not as great as " film effect " which was relatively greater than any other single factor. Moreover, both in reader effect and in unexplained residuum, the variability was lowest when diagnosing clinically significant lesions (and not, as might have been expected, when detecting *any* evidence of

lesions); and variability between readers increased markedly when diagnosing activity. Self-consistency in dual reading—" replication effect "—was associated with relatively low variability, slightly higher in dual reading of small film than of large; on the other hand, inconsistencies between the readings of the three observers were very slightly greater on large films than on small.

SINGLE-CRITERION TABULATIONS. We have so far established the fact that the film-effect was significantly the biggest single factor in contributing to variability in this enquiry. We have now to determine which of the film-type readings was nearer to presenting the truth, and how far readings on one type of film were more accurate than readings on the other. This was done by straightforward tabulations, taking only one criterion at a time. Although tabulations have the disadvantage of considering each criterion in isolation, they are the more usual method of presenting results. They are concerned with comparisons of the different readings with truth, and each tabulation was subdivided into three according to the three criteria of " truly positive " cases:

	1	2	3
" Positive ":	Lesion present (H, F, A)	Lesion clinically significant (F, A)	Lesion active (A)
" Negative ":	No lesion at all (N)	No clinically significant lesion (H, N)	No active lesion (F, H, N)

Separate calculations were made for the findings of (i) the average single reading on small and on large film, and (ii) the average dual reading either by one observer or by two independent observers. Also, the various methods of film reading were combined with different hypothetical procedures in the recall of patients. Thus the tabulations gave estimates of the average " efficiency " of different administrative procedures which might be adopted in chest clinic or mass survey practice. Figs. 1 to 4 illustrate the rates of " pick-up " and " loss " (correct diagnosis and incorrect diagnosis) of truly positive cases, and also the " false positive " diagnoses of true negatives, according to various systems of reading and recall.

Firstly, it will be seen in Fig. 1 that the average *single* reading* on small film detected 77 per cent. of the " truly present " lesions, as compared with 90 per cent. on large film. Similar percentages were reached in diagnosing " clinically significant " lesions. But for " active " lesions the percentages were much lower—only 57 per cent. on small film and 72 per cent. on large. Thus the rate of loss on single large-film reading on the first two criteria—about 10 per cent.—was nearly trebled when radiological diagnosis of activity was attempted.

Secondly, Fig. 2a compares single reading (as already shown in Fig. 1) with dual reading, firstly if carried out by the same observer reading twice, and

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* The average *Single Reading* " pick-up " on one type of film (*e.g.*, on small-film) for any one criterion (*e.g.*, for " lesion present ") is one-sixth of the total number of films correctly diagnosed as " lesion present " in the six individual small-film readings of the three readers.

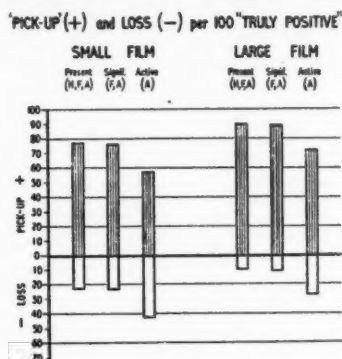I. Average SINGLE READING for EVIDENCE of TUBERCULOSIS

FIG. 1

The average *Single Reading* " pick-up " on one type of film (*e.g.*, on small-film) for any one criterion (*e.g.*, for " lesion present ") is one-sixth of the total number of films correctly diagnosed as " lesion present," in the six individual small-film readings of the three readers.

secondly if carried out by two independent observers.* In dual reading there are two possible methods of recall of patients: " agreement " cases only (++), and " agreement and disagreement " cases (++ and +-).† It will be seen that the " pick-up " rate was consistently higher when recall of " agreement and disagreement " cases was postulated than on recall of " agreement " cases only. If the latter were postulated and dual readings were by two independent observers, the rate of loss of cases with lesions " truly present " was 31 per cent. on small film and 16 per cent. on large; if recall of agreement and disagreement cases were adopted, the loss fell to 15 per cent. on small film and 3 per cent. on large. Similar percentages were lost in diagnosing " clinically significant " lesions. However, the loss of " active " lesions was much greater; with agreement cases recalled, the loss was 60 per cent. on small and 45 per cent. on large film; and with agreement and disagreement cases recalled, the loss fell to 26 per cent. on small and 11 per cent. on large film. It is to be noted also that dual reading carried out by the same observer gave consistently higher loss rates than dual reading by two independent observers.

Thus it can be seen that the " pick-up " rate by dual reading, with recall of agreement cases only, was rather *worse* than the " pick-up " on single reading; and this applied particularly to active lesions. On the other hand, the " pick-up " resulting from dual reading with recall of both agreement and disagree-

* The average *Dual Reading* " pick-up " for *One Observer Reading Twice* on one type of film for any one criterion and one method of recall (*e.g.*, on small film, for " lesion present," " ++ only ") is one-third of the total number of films correctly diagnosed in both readings as " lesion present," in the three observers' own paired small-film readings.

The average *Dual Reading* " pick-up " for *Two Independent Observers* is one-twelfth of the total number of films correctly diagnosed in both readings, in the paired small-film readings of all possible combinations of two different observers.

† " ++ only " means recall of *agreement cases only—i.e.*, when both readings agreed that the case was positive.

" ++ and + — " means recall of *disagreement as well as agreement cases—i.e.*, when one reading only or both readings were positive.

II. SINGLE or DUAL READING for EVIDENCE of TUBERCULOSIS

'PICK-UP' (+) and LOSS (−) per 100 "TRULY POSITIVE"

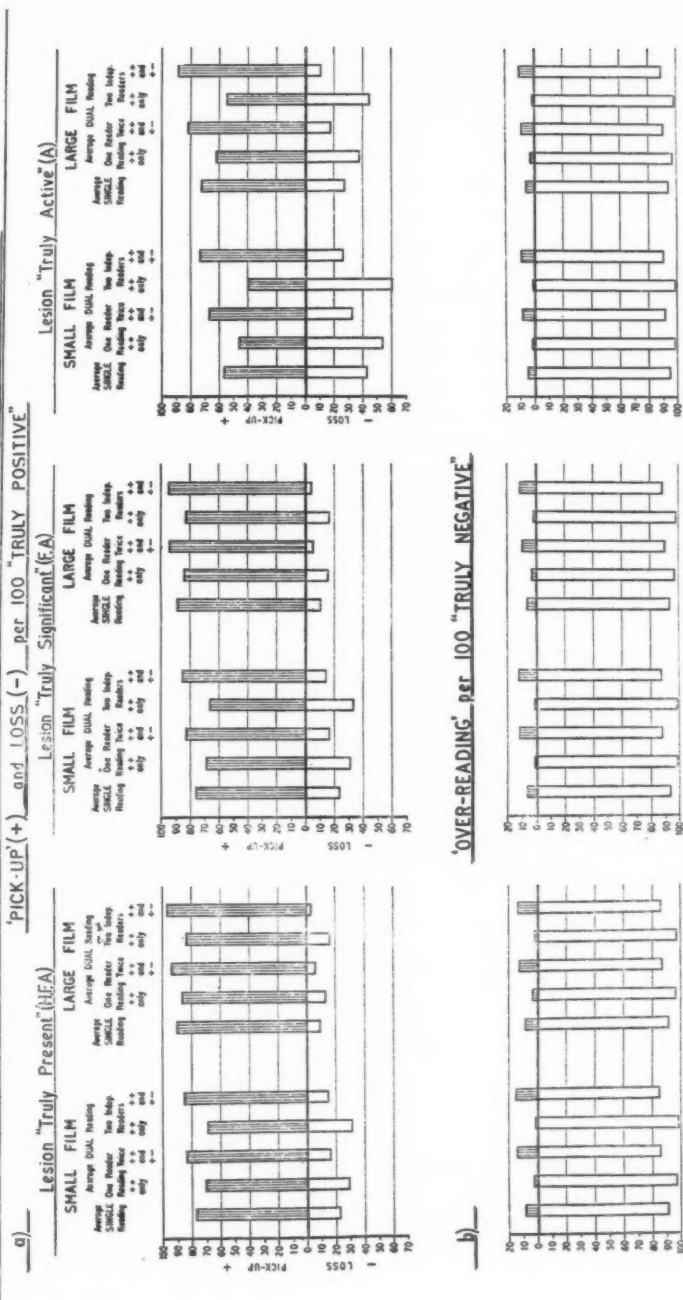'OVER-READING' per 100 "TRULY NEGATIVE"

FIG. 2

The average *Dual Reading* "pick-up" for *One Reader Reading Twice* on any one type of film for any one criterion and any one method of recall (*e.g.*, for "lesion present," ++ only) is one-third of the total number of films correctly diagnosed in both readings as "lesion present," on small-film, in the three readers' own paired small-film readings.

The average *Dual Reading* "pick-up" for *Two Independent Readers* on any one type of film for any one criterion and any one method of recall (*e.g.*, for "lesion clinically significant," ++ and +−) is one-twelfth of the total number of films correctly diagnosed in at least one reading as "lesion clinically significant," in the paired large-film readings of all possible combinations of two different readers.

" ++ only " represents recall of *Agreement Cases Only*; *i.e.*, when both readings agreed that the case was positive.

" ++ and +− " represents recall of *Agreement and Also Disagreement Cases*; *i.e.*, when one reading only or both readings found the case positive.

ment cases was high. Indeed, it should be emphasised that, for active lesions, small film read by two independent observers gave a higher " pick-up " rate than did the average single large-film reading. It seems evident that the benefit of dual reading would be lost if agreement cases only were recalled: but with recall of disagreement as well as agreement cases the small film could be used as efficiently as the present practice of single large-film reading.

With regard to rates of over-reading (false positive diagnoses of cases which were truly negative), it is difficult to compare these with under-reading rates (loss of truly positive cases) or with over-reading rates found in other investigations. Such comparisons would only be valid if the incidence of " truly positive " cases in different populations were the same: for the relationship between " false positive " diagnoses, " loss " of true positives, and correct positive diagnoses depends on the ratio of " true negatives " to " true positives " in the population being surveyed. Moreover, in our enquiry—as also in other investigations—" false positives " were found to vary greatly according to the incidence of *difficult* true negatives (*i.e.*, cases in which there was discrepancy of diagnosis on multiple reading of large film) in the general series of " true negatives." No investigation of the incidence of *difficult* true negatives has been completed, though work on this problem is proceeding (Newell, Personal Communication). Certainly in a series such as ours, drawn from chest clinics, the proportion of " difficult true negatives " was very high. For these reasons, no attempt has been made to estimate an absolute rate of over-reading for use in survey work; the only comparisons which can be made are the proportions of " false positives " per 100 true negatives in our own series, which are comparable between the various systems postulated in this enquiry.

Fig. 2b shows that, whatever the method of reading or the system of recall, over-reading on small film was no greater than on large. In general, the higher the " pick-up " of true positives, the higher was the proportion of " false positives." In dual reading with recall of both agreement and disagreement cases, the proportion of " false positives " per 100 true negatives was approximately double the proportion in single reading.*

Thirdly, Table V shows the " pick-up " rates if 70-mm. film were used for preliminary screening—*i.e.*, if cases were recalled for further investigation

* In one of our chest clinics in 1953, 1,276 referred and contact cases were examined for the first time. The results were as follows:

(a) Cases not recalled for further examination of the respiratory system .. 904
    because: X-rays read clear at first reading   874
                Insignificant tuberculous lesions   8
                Other respiratory conditions   22
(b) Cases recalled as showing lesions or suspected lesions requiring follow-up .. 372
    found to be: Notifiable respiratory tuberculosis   123
                Tuberculosis not notifiable   48
                Other chest conditions   117
                X-rays read clear on second/third reading   84

If we extend some of the results of our investigations to the work of this chest clinic, it seems likely that dual independent reading for " lesion present " and recall of disagreement as well as agreement cases would have resulted in an increase of approximately 24 per cent. (90 persons) in recalls. Since two readings would be needed of large films for all those recalled, as well as of the original small films, the total time required for X-ray interpretation by the clinic staff would have been 2·1 times that employed routinely in 1953. Among the additional recalls which have been estimated, it would have been expected that approximately 17 cases of tuberculosis (13 notifiable) would be discovered.

TABLE V.—DETECTION AND ACCURACY OF DIAGNOSIS OF "TRULY POSITIVE" CASES OF TUBERCULOSIS

("Truly Positive" according to three different criteria)

IN SINGLE AND DUAL READING OF SMALL FILM (70-MM.) AND LARGE FILM (STANDARD)

Dual Reading: "++only" means cases for which both readings agreed that case was positive
"++and+−" means cases for which one or both readings found case positive

"Pick-up" rate per 100 "True Positives" i.e., Cases actually read "positive" among all those which were agreed "positive" at subsequent "Truth Sessions."	Per 100 cases with evidence of tuberculosis "Truly Present" (H, F and A)					Per 100 cases with tuberculosis "Truly Clinically Significant" (F and A)					Per 100 cases with tuberculosis "Truly Active" (A)				
	Average* single reading	One observer reading twice†		Two independent observers‡		Average single reading	One observer reading twice		Two independent observers		Average single reading	One observer reading twice		Two independent observers	
		++only	++and+−	++only	++and+−		++only	++and+−	++only	++and+−		++only	++and+−	++only	++and+−
Small-film for screening or for definite diagnosis: Film read for "Tb Present"	77·1	70·5	83·7	69·0	85·2	82·8	77·2	88·4	76·0	89·6	85·9	80·6	91·1	79·8	92·0
Film read for "Tb Clinically Significant"						76·0	68·7	83·3	66·7	85·4	79·1	72·1	86·1	70·7	87·4
Film read for "Tb Active"											56·8	46·1	67·4	39·8	73·7
Large-film for definite diagnosis: Film read for "Tb Present"	90·2	86·4	94·0	83·8	96·7										
Film read for "Tb Clinically Significant"						89·3	84·0	94·6	83·0	95·7					
Film read for "Tb Active"											72·1	62·0	82·2	55·3	88·9

* The average *single* small-film reading for "tuberculosis present" is one-sixth of the total number of films correctly diagnosed as "tuberculosis present," in the six individual small-film readings.

† The average *dual* small-film reading for one observer reading twice for "tuberculosis present," ++ cases only, is one-third of the total number of films correctly diagnosed in both readings as "tuberculosis present," in the three observers' own paired small-film readings.

‡ The average *dual* small-film reading for two independent observers for "tuberculosis present," ++ cases only, is one-twelfth of the total number of films correctly diagnosed in both readings as "tuberculosis present," in the paired small-film readings of all possible combinations of two different observers.

whenever the presence of a lesion was detected in small-film readings; the final diagnosis in regard to " activity " would then be decided in subsequent large-film readings. Thus, if radiological diagnosis of " activity " were attempted from a single small-film reading, only 56·8 per cent. of truly active cases would have been correctly assessed. On the other hand, the average single small-film reading detected 77·1 per cent. of cases with a lesion " truly present," and within these there were included 82·8 per cent. of all " truly clinically significant " lesions and 85·9 per cent. of all " truly active " lesions. If these cases were recalled for large-film examination and definite diagnosis, only 72·1 per cent. of them would have been correctly assessed as " active " in the average single reading—giving a final " pick-up " of 61·9 per cent. (85·9 by 72·1) of all truly active cases. In this way, by multiplying the appropriate percentages, it is possible to make estimates of the combined pick-up rates according to different methods of using 70-mm. film for preliminary screening and large film for recalled cases.

The optimum procedure for finding active cases—small film read twice for " lesion present " by two independent readers, with recall of both agreement and disagreement cases—detected 92 per cent. of the active cases; and the optimum procedure in subsequent large-film reading—dual reading by two independent observers—correctly diagnosed 88·9 per cent. of the active cases

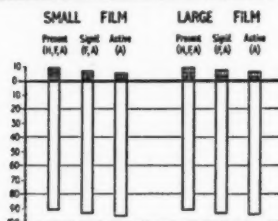III. Average SINGLE READING for "MINIMAL TUBERCULOUS LESIONS" and "TUBERCULOSIS, OTHER STAGES"

a) PICK-UP and LOSS per 100 "TRULY MINIMAL"
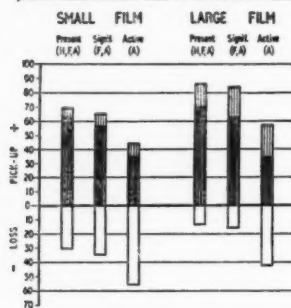
PICK-UP and LOSS per 100 "TRULY OTHER STAGES"
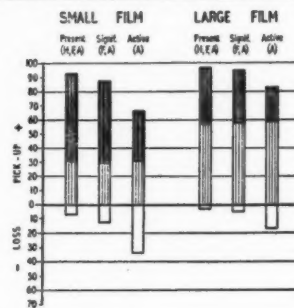
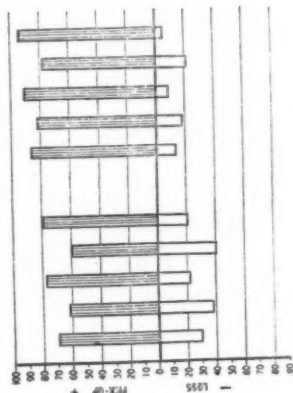b) "OVER-READING" per 100 "TRULY NEGATIVE"

IV. SINGLE or DUAL READING for MINIMAL LESIONS

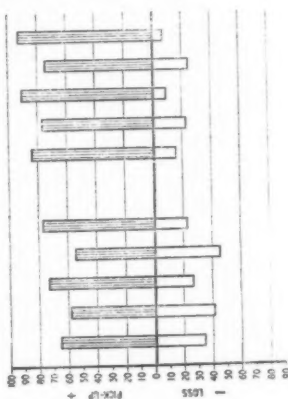'PICK-UP' (+) and LOSS (−) per 100 "TRULY MINIMAL"

amongst those recalled if disagreement as well as agreement cases were taken. Thus the final pick-up would have been 81·7 per cent. of all truly active cases. Even if a less precise diagnosis were aimed at, and the preliminary screening by small film were carried out for " lesion present " and the subsequent large film were used to identify clinically significant lesions (whether active or not), the final pick-up by the optimum procedure would still only be 85·7 per cent. of all truly significant cases.

The foregoing rates and diagrams have described the rates of pick-up and loss in regard to all types of lesions. Figs. 3 and 4 illustrate the corresponding rates for " minimal lesions " and " tuberculosis, other stages " considered separately. Briefly, these diagrams demonstrate—as one might expect—that the pick-up of minimal lesions was rather less than of " tuberculosis, other stages "; the differences are seen to be fairly consistent, whether small or large films were being read. The loss of " minimal lesions " on dual reading was rather greater than the averages shown in Figure 2 and Table V; and when diagnosis of " activity " was attempted, even on large film reading, the loss of cases with minimal lesions was more than 40 per cent. on single reading and more than 20 per cent. on dual reading by two observers.

Discussion

For those of us engaged in clinical and radiological work the personal experience gained in participation of this investigation has been revealing and salutary. A recent leader in the *Lancet* (1954) concluded: " It is astonishing how widely interpretations may vary; and anyone who fancies that this applies only to his colleagues should be urged to participate in an observer-error test as a chastening experience." Our investigation has taught us how often film reading—whether large or small—fails as an instrument of diagnostic precision; how surprising are the differences in our own judgment on a given film at different times; and how divergent are the assessments that we, and others equally experienced and competent, make on that film. The same leader in the *Lancet* suggested, however, that special enquiries such as ours, imposed on the participants one condition which is not routine practice. Readers were asked to avoid tentative opinions and to record firm decisions on each film. They could not defer final interpretation of a suspicious shadow till a second film and further clinical observation became available, nor had they any previous clinical history to supplement their radiological diagnosis.

At first sight this necessity for making immediate firm decisions might be thought to increase in some measure the inter- and intra-observer variability. Indeed, it is a widely held belief that observer-variability and loss of true cases demonstrated in special investigations would not occur under normal working conditions in which clinical and family history and the like can supplement radiological findings. We would point out that in mass survey work and in clinics examining contacts, positive radiological findings are the starting-point for clinical and bacteriological examination; without positive radiological findings, no supplementary evidence is sought. Thus the pilot enquiry which we have carried out corresponds very closely with normal working conditions in the diagnosis of minimal tuberculosis, especially as we have postulated several different administrative and follow-up procedures.

Moreover, data are now available on observer-variability and loss of true cases in dual reading carried out in practical work. In Denmark in 1952 dual reading was introduced in mass X-ray surveys, the second reading being made by a central reader independently of the usual reading by the local senior chest physician. Groth-Petersen and Møller (1953) found that the central readers added nearly 20 per cent. of *active* tuberculosis and 44 per cent. of other significant pulmonary conditions to the cases detected by the local readers. However, central as well as local readers overlooked a considerable number of significant pulmonary changes. Among the active tuberculosis cases missed by one or other reader the type of case was closely similar to the type of case detected by both readers; 86 per cent. of the missed cases had tubercle bacilli at first examination of sputum or gastric lavage, 35·5 per cent. had bilateral processes, and 15·5 per cent. had cavities. These data strongly suggest that the findings of special investigations are borne out by practical mass survey and clinic work, and observer-variability and loss of true cases are as high under normal working conditions as under conditions of special enquiries.

Self-Consistency. Our results indicate, perhaps contrary to expectation, that there is no great improvement in our self-consistency or in our agreement with others when we are dealing with large as opposed to small films. Consistency was slightly worse for small films in this pilot enquiry, but this may have been due to two factors. Firstly, we were less experienced with small film than with large. Secondly, as explained above, it was during the circulation of small films that discussions took place which might have increased discrepancies between first and second small-film readings, whilst having the opposite effect in the large films. However, consistency was not good even on large film, and in particular we would stress the poor consistency, whether with oneself or with others, in the assessment of " softness " or " activity."

We found, as might have been expected, that there was greater divergence between observers' than within an observer's own readings. It was striking that this divergence was as great on large as on small film. But it was even more striking (and hopeful) that the difference within observers' own readings on different types of film was comparatively small. It seems to us possible that increased consistency could be achieved by more systematic training in the interpretation of chest films. Whether, in addition, objective aids such as standard films would have the same value in tuberculosis as they have in pneumoconiosis seems doubtful, in view of the widely varying behaviour of the early tuberculous lesion. Though gross and excavated disease presents few problems, we have seen how very difficult it is to achieve uniformity in the detection of the very small changes.

The Loss of " Positive " and " Active " Cases. Our tables and diagrams show that on the criterion of the presence of tuberculosis the average single small-film reading detected 77 per cent., but that on the criterion of activity the corresponding figure was only 57 per cent. For the single large-film reading the percentages were better, but the relative demerit of the criterion of activity was just as evident. This gives cause for serious concern in the loss of truly active cases in present clinic work where it is sometimes the practice to diagnose activity on large films.

We have shown that, if the practice adopted were to recall only those cases

where the dual readings (either by one reader or by two independent readers) *agreed* on activity, the loss of positive cases would be considerably increased. If, on the other hand, the practice of recall were based on a positive finding on *either* of the two independent readings, the loss would be substantially reduced. However, we have demonstrated that, if small film were used purely for screening purposes and subsequent large films were taken for all recalled cases, even the combination of optimum procedures of independent readings on both small and large film would result in a loss of more than 18 per 100 truly active cases, or more than 14 per 100 clinically significant cases.

In this connection it should be stressed that the independent reading by a second observer must be really independent. This condition is not fulfilled by the reporting of a film by a junior immediately after his senior has read it, and perhaps in the presence of that senior. Moreover, when a junior has been entirely trained in one chest service, his reading may be hardly more independent than the repeat reading of his senior. How far the necessity for two completely independent readers to assess small and large films could be relaxed by the development of an over-riding objective standard of film reading is at present a matter for conjecture.

Recall of " False Positives." We have to consider not only the greatly improved diagnosis of true cases achieved by dual reading by two readers, but also the counterbalancing effect of the unnecessary recall of " false positives." Previous enquiries as well as our own have shown that the unnecessary recalls increase with dual reading and especially with the recall of disagreement as as well as agreement cases. Groth-Petersen and Møller (1953) showed that in dual reading of 35 mm. film in mass surveys, the second readers added 48 per cent. to the " false positives " unnecessarily recalled for a large film (and, as previously mentioned, added 41 per cent. to the true positives discovered). In our enquiry the proportion of "false positives " (on the criterion of clinically significant lesions) was 6 in every 100 true negatives on single small-film readings and over 11 in every 100 true negatives on dual readings. On large-film readings, the percentages were very similar.

It should be emphasised that our proportions of " false positives " are not comparable with the proportions found in other investigations, for two reasons. Firstly, if a series has a very low incidence of true positives (as in mass surveys) the proportion of true negatives is high and these are, of course, all subject to being falsely diagnosed positive. In our own series, on the contrary, the proportion subject to false positive diagnosis was much lower than it would be in a normal population, and therefore our results on over-reading would require to be standardised for this disproportion, on the basis of some " expectation of normal incidence " of tuberculosis. Indeed, the " false positive " rates found by other investigators may all apply to quite different populations and not be comparable with each other. Nevertheless each is doubtless useful for administrative practice in the population to which it applies, though for comparisons or for assessment of efficiency each would require to be adjusted to some standard population with a given incidence of tuberculosis.

" *Difficult True Negatives*." Secondly, there is a more important consideration in regard to " false positives," namely the occurrence of " difficult " true negatives within the general series of true negatives which are subject to false

positive diagnosis. In our series approximately only half of the " true negatives " were read as negative by all readers at all times. The over-reading occurred in a group of true negatives which were in the main difficult to read, and in many of which the fact of being negative was only decided after lengthy discussions at " truth sessions," requiring follow-up films and case notes. This may be due to the fact that these cases came from a special type of population, namely referred cases and contacts at chest clinics. On the other hand, Groth-Petersen's and Yerushalmy's series came mostly from mass surveys of the general public with a low incidence of tuberculosis and almost certainly a low incidence also of " difficult " true negatives. Variations in such incidence are likely to be great, depending on the nature of the population, on age and sex composition, on incidence of other respiratory disorders, on exposure to contact, and so on. It is our opinion that the incidence of " false positives " should be assessed on the basis of the incidence of " difficult true negatives " in which there is dis-crepancy of interpretation on multiple readings, and not simply on the total incidence of " true negatives " alone. Little is known at present about this incidence; moreover, the exclusion of " questionable " cases (Groth-Petersen, Yerushalmy, etc.) from analyses is likely to give too favourable a picture of the incidence of " difficult " true negatives.

In the light of these considerations, physicians and radiologists engaged in chest clinic work will have to balance the disadvantage of single X-ray readings (loss of genuine cases) against the disadvantage of dual X-ray readings (excessive recall of " false positives "), which would be even more marked if small film were used for preliminary screening only. It may be that unnecessary recall of false positives after dual reading of small films would be a big enough factor in chest clinic work to make it uneconomical to use small film: in mass survey work, of course, small film would be essential, but in chest clinics dual independent reading of the full-size X-ray for all cases might save more time and work than it would cost in money. If our results are confirmed by the second and larger investigation now in progress, the tuberculosis service will be confronted with the choice of recognising that a considerable number of early cases are missed by present methods, or of radically reorganising their case-finding programmes.

Summary

The main object of this enquiry was to assess the success of 70-mm. film in the detection of tuberculous lesions. Integral to such an object were (i) assess-ments of the nature and magnitude of discrepancies by the same observer at different times and by different observers in judging such film: (ii) similar assessments in respect of *large* film: and (iii) the decision as to the presence and " true " nature of any lesion (" truth " session). The plan of the enquiry, moreover, has enabled us to contrast the advantages and disadvantages of different practices of film-reading and different procedures in recall of cases that might be introduced in routine radiographical work.

The main results of the investigation were these:

1. Irrespective of size of film, *variability* (*i.e.*, inconsistency in readings,

regardless of " truth ") was appreciably lower in successive judgments by the same reader than it was between those of different readers.

2. Within-reader variability was nearly as great with large film as it was with small. Between-reader variability was, if anything, greater on large film than on small.

3. *Accuracy* (*i.e.*, agreement with " truth ") was better in readings of large film than of small, but even on large-film readings loss of genuine cases was considerable.

4. Accuracy decreased when attempts at increased precision of diagnosis were made, and was especially low in attempted diagnosis of " activity " of lesions.

5. Accuracy was worse in the detection of *minimal* lesions than of " tuberculosis, other stages "; but inaccuracy in judgments of activity was striking, even with lesions more advanced than minimal.

6. Comparison of the relative efficacy in detecting positive cases by single and dual readings of film showed that the *optimum* result was obtained by *independent dual* reading together with follow-up of cases called positive on *either or both* readings; the *worst* by consideration only of those cases called positive on *both* readings.

Dual small-film reading by two independent observers, with follow-up of disagreement as well as agreement cases, gave as good a result as did single large-film reading (though not as good as independent dual large-film reading).

7. With a combination of preliminary small-film screening and follow-up large-film diagnosis, the *optimum* procedure elicited less than 82 per cent. of active lesions and less than 86 per cent. of clinically significant lesions.

8. " False positive " readings were produced in as high a proportion of large-film readings as of small, whatever the method of reading. With dual reading, the increased pick-up of true cases was accompanied by an appreciable increase in false positives. In general, the methods producing the more successful pick-up of genuine cases produced also a higher proportion of unnecessary recalls.

9. The frequency of " false positive " readings depends on the real incidence of tuberculosis in the population surveyed and also on the incidence therein of " difficult true negatives." For this reason the proportions of " false positives " recorded here are not compared with those of previous investigations.

10. As a result of these initial findings, the following *recommendations* seem worthy of presentation here:

No patient attending a chest clinic should be dismissed as normal unless, in addition to negative clinical findings, the chest X-ray has been scrutinised independently by two readers who both report no evidence of respiratory disorder.

It is inadvisable to attempt the diagnosis of activity from X-rays, especially in the case of a minimal lesion.

There is need for systematic training in the reading of films and for the investigation of the possibility of mechanical and objective aids to consistency in film reading.

For mass surveys, small film could be used as efficiently as standard X-ray

if " presence " of a lesion is taken as the only criterion and no attempt to assess significance or activity is made. In chest clinic work, the time and work involved in dual readings of small film followed by dual reading of large film for all recalled cases might be less economical than the use of large film from the outset.

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PRINCIPLES IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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Introduction

THE advent of effective chemotherapy revolutionised the treatment of pulmonary tuberculosis and led directly to the recent dramatic fall in mortality.

In pre-chemotherapeutic days, medical treatment had left much to be desired. The follow-up of patients treated by sanatorium régime revealed a high rate of relapse and of mortality (with the exception of results achieved by a few selective institutions). Apart from bed rest artificial pneumothorax was the usual form of active treatment. This procedure was used, all too frequently, on the wrong type of case, at the wrong moment, and results were often poor. Empyemata were frequent and the help of the surgeon was enlisted to rescue the patient from the failure of the physician.

The thoracic surgeon thus gained an ascendancy over the physician, both in this and in other countries. Chemotherapy was welcomed by the surgeon and encouraged him to extend his field of operations. It has even been suggested that surgery is the proper and most efficient treatment of pulmonary tuberculosis.

This work grew from a desire to discover the reason why medical treatment had failed, for if the cause of failure could be found, it should be possible to adopt measures leading to success in treatment.

Whilst mortality from respiratory tuberculosis has fallen dramatically, there has been no appreciable fall in the number of new cases per annum in England and Wales. The new cases (all forms of tuberculosis) reported in 1953 were 43,984. Of these 16,495 were reported to have sputum positive. (If comprehensive bacteriological search had been general throughout the country the number of sputum-positive cases would probably have been approximately 20,000.)

The average new cases, per annum, from 1936 to 1940 were 40,000 (Annual Report of the Chief Medical Officer of the Ministry of Health, 1953).

The M.R.C. Tuberculin Survey (1952) revealed that the annual tuberculous infection rate amongst young people was more than doubled in the years immediately after leaving school. This gave evidence of the widespread existence of infection in offices, workshops and factories. So long as chronic carriers of tubercle bacilli are permitted to work in normal industry, so long will the problem of treatment remain with us (20,000 patients per annum).

THE EVOLUTION OF TUBERCULOUS CAVITIES

The role of coughing, in the development of phthisis, aroused interest in the search for effective medical treatment. It was noted, on many occasions, that

excessive coughing led to a marked increase in excavation and to spread of disease. Conversely, patients with little or no cough showed improvement. Study of this aspect of the disease converged on the works of Coryllos, particularly his views on the mechanics of cough, and on the mechanics and biology of tuberculous cavities (Coryllos, 1936 a and b).

Cavities represent the most important feature of pulmonary tuberculosis. " In fact they are the laboratories in which the tubercle bacillus lives and grows and its metabolic products develop, causing both local and general symptoms of phthisis. Chronic pulmonary tuberculosis without cavities is a quiescent and benign disease; with cavities it is a progressive and malignant one."

Following the inhalation of tubercle bacilli, a lesion will develop adjacent to a small bronchiolus, the lumen of which becomes narrow and more or less obliterated by cellular proliferation. Caseous necrosis develops, the cells obstructing the bronchiolus are liquefied, and the tuberculous exudate is passed into the bronchial tree and evicted as sputum.

By the liquefaction of the tubercles a cavity is formed, in communication with a bronchus.

" This hole does not collapse, as would occur in any other organ, because the lung contains air, and because of the difference of pressure inside and outside of the lung. In fact, in the bronchi the pressure is equal to one atmosphere, while outside of the lung the pressure is subatmospheric and equal to the negative intrapleural pressure. For the same reason the cavity assumes a spherical shape in the living patient, while it appears irregular at the autopsy table, following the opening of the chest which suppresses the negative intrapleural pressure. Thus a cavity is spherical because the pressure inside of it is higher than around it, exactly as an abscess or cyst is spherical because it is filled with pus or fluid under tension."

Coryllos maintained that the bronchial outlets, or draining bronchi, represent the most important factor in the development of cavities. Changes in the lumina of the bronchi, especially their closure, must influence the further evolution of cavities. When air is trapped anywhere within the body (*e.g.*, in the pleura or peritoneum) it is finally absorbed by the circulating blood. Obstruction of a pulmonary bronchus is always followed by absorption of air contained in the corresponding portion of lung and atelectasis is produced.

The disease process will cause narrowing of the bronchial lumen, and obstruction which may be temporary or permanent.

Three eventualities may occur: (1) the bronchial outlets of a cavity may remain open, (2) they may become narrowed, or (3) they may close (see Fig. 1, after Coryllos).

In the second case a one-way valve mechanism will develop which allows ingress of air during inspiratory expansion of the bronchus, whereas during expiration obstruction becomes complete and air is trapped within the cavity. With successive inspirations more air is trapped and the cavity becomes larger.

Few clinicians appreciate the significant role of coughing in the formation and development of cavities.

The excessively deep inspirations, preceding each cough, contribute more than any other factor to the increase in the size of cavities, as outlined above.

In the third case, if the draining bronchus is obstructed, the air within the

cavity will become absorbed. The cavity will shrink and finally disappear, leaving little or no trace. This simple conception explains the beneficial effect of bed rest, which decreases the need for oxygen by the body and consequently decreases the amount of the respiratory expansion of the diseased bronchi. During quiet, minimal respiration, the bronchi will remain shorter and more contracted.

Artificial relaxation therapy (*e.g.*, pneumothorax or pneumoperitoneum) may enhance the value of bed rest, in favouring the collapse and closure of the bronchial outlets of the cavities.
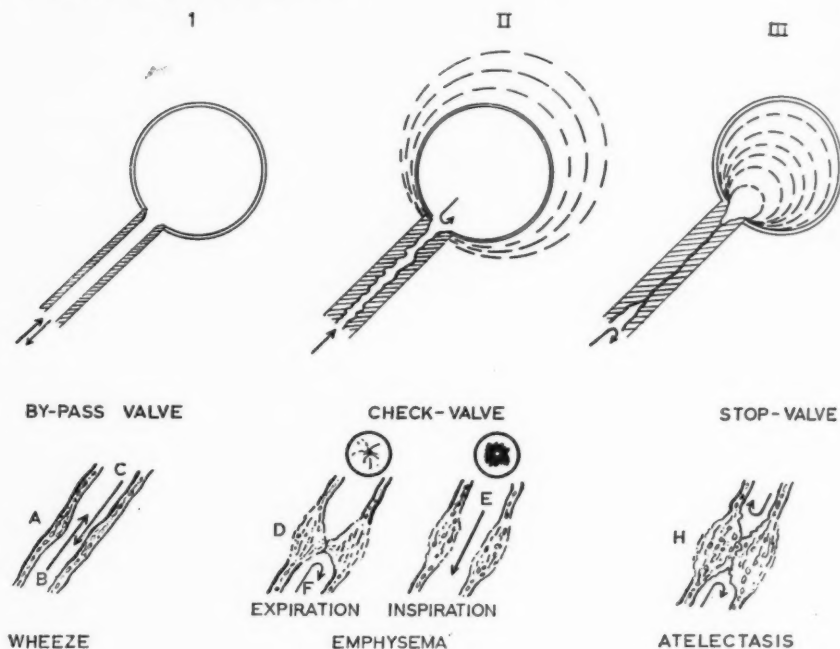
FIG. 1.—After Coryllos.

Coryllos also stressed the biological effects of the closure of the draining bronchus upon the tubercle bacilli contained in a cavity. The human tubercle bacillus is a strict aerobe. Suppression of oxygen for a few days only will impair its respiratory metabolism and lead to its death.

Another biological effect of the closure of draining bronchi and the atelectatic shrinkage of cavities and of the surrounding lung parenchyma is the development of fibrous tissue.

" Thus the cycle of events leading to the arrest of disease is complete: closure of bronchial outlets, disappearance of cavities, negative sputum, arrest of development of toxic products, with clinical improvement of the patient and fibrosis of the lung. The links of this chain are solidly riveted, and none of these can be suppressed without destroying the succession of events. All phenomena occurring in the course of the disease are thus clearly explained by simple

physiological, mechanical, physiochemical and bacteriological facts which are well known and firmly established. There is no need for involved or meta-physical theories."

The clinical cure of pulmonary tuberculosis can best be achieved by slowing down pulmonary ventilation, and thus decreasing or suppressing the oxygen necessary for the continuation and growth of tubercle bacilli.

The conceptions of Coryllos were simple (perhaps too simple) and have been little appreciated. Ellman (1939) reported the tendency of certain tuberculous pneumonic and bronchopneumonic lesions, with or without cavities, to heal spontaneously. Impressed by the rational explanation of Coryllos and Ornstein (1938) he noted the desirability of strict, and subsequently modified, bed rest and stressed also the importance of complete co-operation of the patient.

Treatment on these lines was utilised some years before the advent of chemotherapy. I have previously reported (Toussaint, 1952) a series of 196 cases treated at home, between 1.9.46 and 30.6.49, with prolonged bed rest, aided by relaxation therapy. The latter was initiated in the patients' homes. This series of cases is grouped in Table I. Disease was progressively more severe in Groups B, C, D and E.

TABLE I.—DOMICILIARY RELAXATION THERAPY
Total 196 Cases. Treatment started between 1.9.46 and 30.6.49

		Cases	Admitted to sanatorium Cases
Group A.	Treated by artificial pneumothorax	70	11
Group B.	Treated by diaphragmatic elevation followed by A.P. on same side	19	5
Group C.	New cases treated by diaphragmatic elevation	37	—
Group D.	Relapsed cases treated by diaphragmatic elevation ..	17	—
Group E.	Treated by diaphragmatic elevation followed by sana-torium	53	53
		196	69

Collapse therapy was accompanied by prolonged bed rest in all cases.
Sanatorium beds saved 127.

A large majority of the whole series were treated before the general release and adoption of streptomycin and P.A.S. Of the total only 69 were admitted to sanatoria, and of the remaining 127 none were treated by chemotherapy.

The condition of these patients on June 30, 1954, is shown in Table II.

The final results, with a high percentage of cases arrested, have fully justified the methods used in this series. The subsequent advent of chemotherapy and the use of " postural " rest have markedly improved the prospects of effective medical treatment.

Based on past experience, the following principles have been evolved:

First Principle—Bed rest. Prolonged and absolute bed rest is a rule. The object in each case is to maintain respiration at a minimal level and thus to help the bronchus, draining a cavity, to contract and become occluded. Even with a

TABLE 2.—DOMICILIARY RELAXATION THERAPY

196 Cases. Treatment started between 1.9.46 and 30.6.49. Condition on June 30, 1954

Group	Disease arrested Working	Disease arrested	Disease stationary (still active)	Dead	Total
A.—A.P...	58	2	5	5	70
B.—P.P. and A.P.	16	—	2	1	19
C.—P.P. (new) ..	25	1	2	9	37
D.—P.P. (relapse)	6	—	4	7	17
E.—P.P. and San.	30	3	6	14	53
	135	6	19	36*	196
	Total arrested 141 =72%				

* 2 of these deaths due to bronchial carcinoma.
1 of these deaths due to œsophageal carcinoma.

small lesion, if tubercle bacilli are present in the sputum, it is best to maintain strict bed rest for six months.

Enforced bodily rest must be accompanied by mental rest. This is secured by close collaboration with the Almoner, to whom each new case is referred on diagnosis. The Almoner's help is invaluable in allaying the anxieties and apprehensions which follow the disclosure of a serious illness.

Second Principle—Complete elimination of cough. The easiest way to secure this is by adequate instruction of the patient. Cough is originally induced by the presence of sputum within the bronchial tree. It then becomes a habit and the patient coughs without noticing he is doing so. A vicious circle will ensue and the cough soon becomes excessive.

Each patient is given a short explanation of the disease process in simple terms. The role of coughing in the maintenance of cavities is emphasised. The patient is told firmly that, for his own good, he must stop coughing. Most patients have stopped quite soon.

To assist in the cessation of cough drugs are of value in the first two or three weeks. During this time Tab. Dicodid gr. ⅛, night and morning, was very useful. Its use can be abandoned after two weeks.

The bronchi must be kept free from any irritation. For this reason smoking is *prohibited*. However little a person may smoke this act will maintain coughing. From the experience gained there is no doubt that the patient who stops smoking will fare better than he who will not. It is time the profession realised the deleterious effect of smoking upon tuberculous ulcers in the lung.

In a few patients trouble is experienced from bronchial spasm. If this is not relieved cough will persist to some extent. In such cases benefit is obtained by the use of antispasmodics and/or antihistamines. Bronchial spasm may also be relieved by chemotherapy.

Third Principle—Use of posture. Still better results can be obtained if bed rest is modified by posturing the patient, in such a manner that excavation is in the most dependent part of the thorax.

PLATE VIII
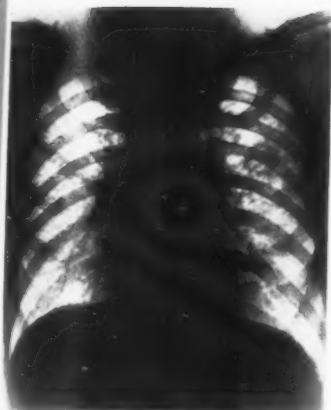
CASE 1.—(a) 27.7.51. M. 35 yrs. Sp. +. Posture, L. side for 3 months. Chemotherapy; 42 gm. Strep. and P.A.S., followed by P.A.S. and T.B.1. for 2½ months.

CASE 2.—(a) 26.2.54. M. 26 yrs. Sp. +. Wt. 12 st. 2 lb. Posture, R. side for 4 months. Chemotherapy: Strep. 105 gm. and I.N.A.H. (200 mgm. daily).

(b) 29.10.51. Cavity closure in 3 months. Tomo: no excavation. Sputum cult. Neg. L.A.P. induced 6.11.51, L.A.S. 14.12.51. Discharged hospital 9.1.52.

(b) 19.5.54. Cavity obliterating. L.A.P. 1.6.54, L.A.S. 2.7.54. R.A.P. 31.8.54, R.A.S. 1.10.54.

(c) 5.8.52. Good L.A.P. Well and working.

(c) 14.12.54. Wt. 14 st. 2 lb. Symptomless. Good bilateral A.P.s.

PLATE IX
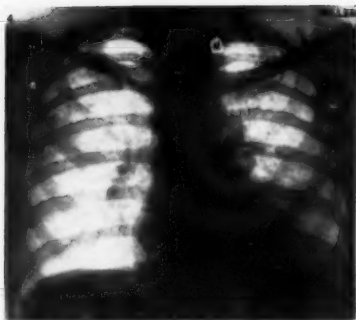
CASE 3.—(a) 7.7.52. F. 23 yrs. Sp. ±. Wt. 7st. 2 lb. Posture, L side, 3 months. Cavity closure (L. apex) 3 months. Chemotherapy: Total 45 gm. Strep. and P.A.S. R.A.P. (free) 8.10.52. L.A.P. 13.12.52. L.A.S. 5.2.53. Both A.P.s stopped 16.2.54. Progress excellent.
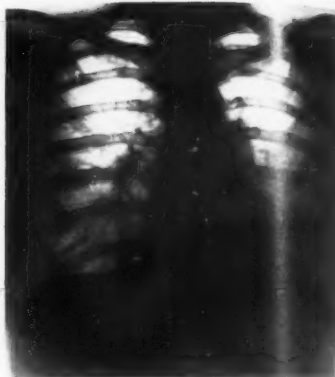
CASE 3.—(b) 4.11.54. Wt. 10 st. 1 lb. Lungs clear of disease. Pregnant, following agreement by physician. E.D.D. March 1955.
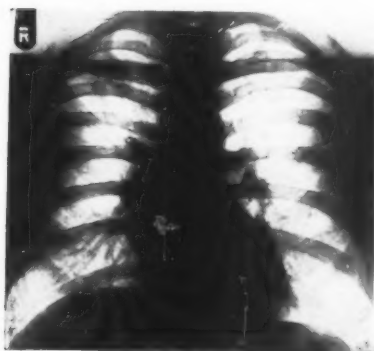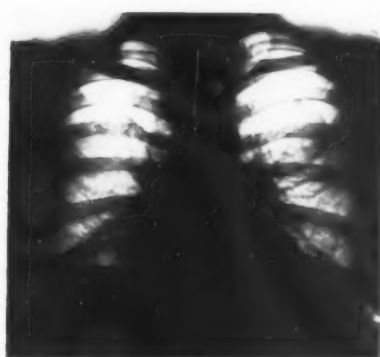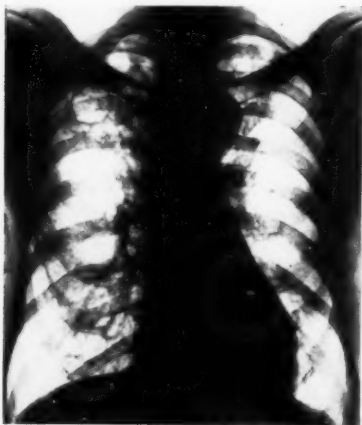

CASE 4.—(a) 9.1.52. M. 62 yrs. Sp. +. Wt. 9 st. 5 lb. Posture, R. side for 4 months. Hospital 6 months. Chemotherapy: Strep. 54 gm. and P.A.S. followed by T.B.1. 100 mgm. daily for 5 weeks.
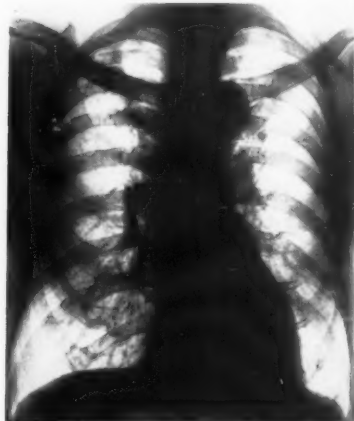
CASE 4.—(b) 13.1.54. Wt. 11 st. Well. Working 45 hours per week in factory.
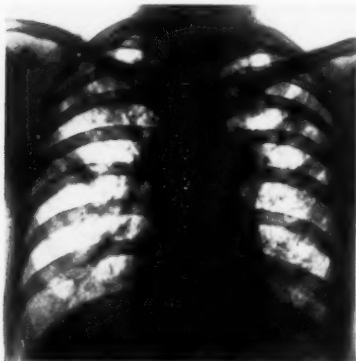
CASE 5.—(a) 16.6.50. F. 30 yrs. B.S.R.92. Wt. 8 st. 11 lb. Sp. +. Extensive bilateral disease with excavation in both upper zones. Postured, on back, 4 months, bed 6 months. Chemotherapy: Strep. 40 gm. and P.A.S. Undertaking light housework in 1 year.
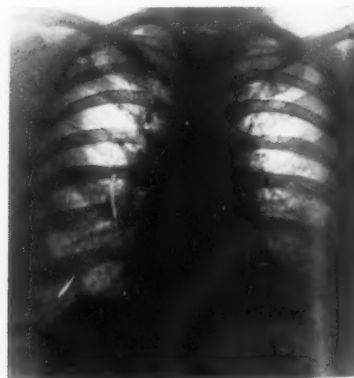
CASE 5.—(b) 22.3.54. Wt. 10 st. 11 lb. Well. Full duties as housewife. Lungs clear of active disease.

In many patients there is a single large cavity in the right or left upper zone. In such cases " postural treatment " is gained by raising the lower end of the bed and keeping the patient over on the side of the cavity. This position is maintained day and night, except for the short time of meals and toilet. In this position the weight of abdominal viscera will raise the dependent leaf of the
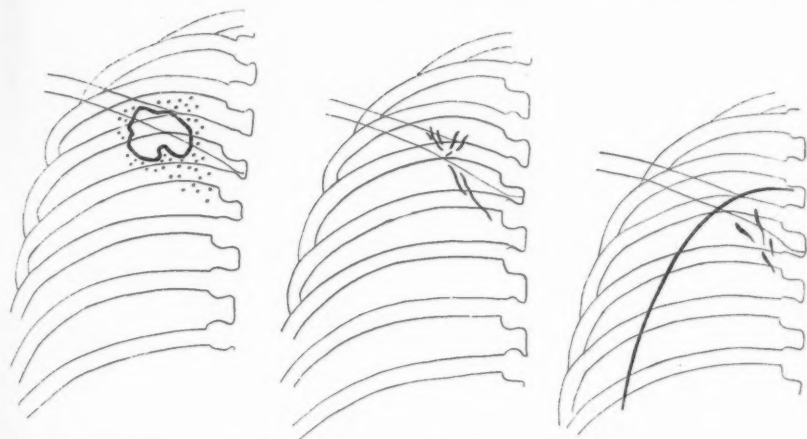
CASE 6.—(a) 16.2.54. F. 18 yrs. Sp. +. Wt. 9 st. 5 lb.
    (b) 20.5.54. Cavity closure after 3 months' posture, R. side. Chemotherapy: Strep. 84 gm. and I.N.A.H. (12 weeks).
    (c) 8.7.54. R.A.P. 16.6.54. R.A.S. 16.7.54.
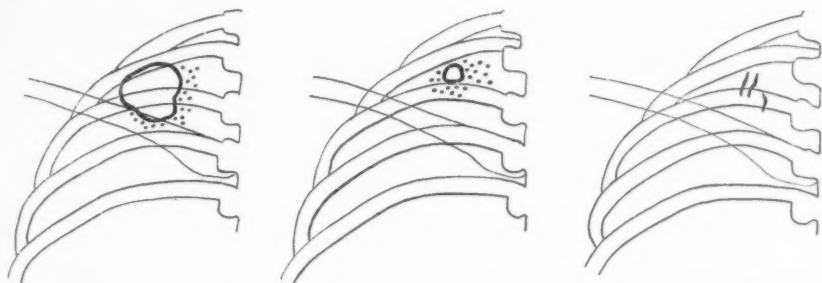
CASE 7.—M. 33 yrs. Drawings from Tomo (8 cm.) 30.4.52, 25.7.52, 26.9.52. Posture, R. side for 5 months—cavity closure. Chemotherapy: Strep. 60 gm. and P.A.S. followed by I.N.A.H. and P.A.S. for 10 weeks. R.A.P. 2.10.52 to 15.12.53. October 1954. Well and working.

diaphragm well up into the thorax. The heart and mediastinum tend to fall to the lower side and the ribs on that side remain close together. Finally the lower or dependent lung is relaxed to a very much smaller volume than usual. The effect is much the same as that obtained by a phrenic crush and pneumo-peritoneum. In fact, the latter procedure has been used less since the adoption of posture.

Patients with bilateral upper zone disease are postured, with foot of bed

raised, flat on their backs. Initial treatment of mid and of lower zone cavities is undertaken with the bed flat, and the patient also flat on his back.

Many amazing examples of cavity closure have been obtained (see cases 1 to 9).

Postural rest has been advocated, with enthusiasm, by Dilwyn Thomas, Dormer *et al.* (1951), and Aslett and Erin (1952).
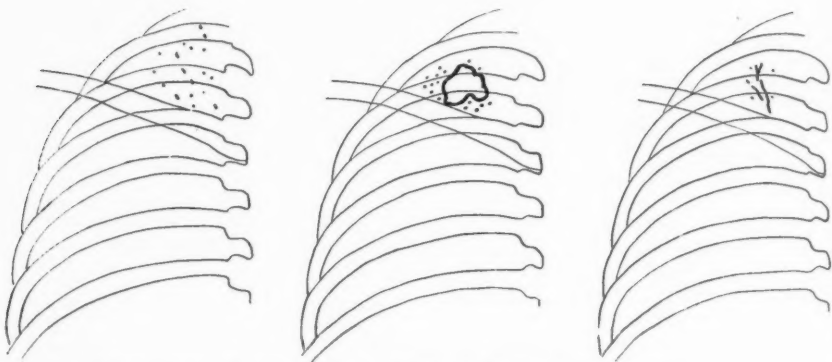
CASE 8.—(*a*) 22.12.52. F. 21 yrs. X-ray: Minimal disease R. apical region.
(*b*) 27.12.52. Tomo: revealed irregular-shaped cavity. Posture, R. side, 4 months, bed 5 months. Chemotherapy: Strep. 42 gm. and I.N.A.H. Tomo: 29.4.53—cavity closed.
(*c*) 3.2.54. Tomo: same cut—no excavation. Patient well and working.
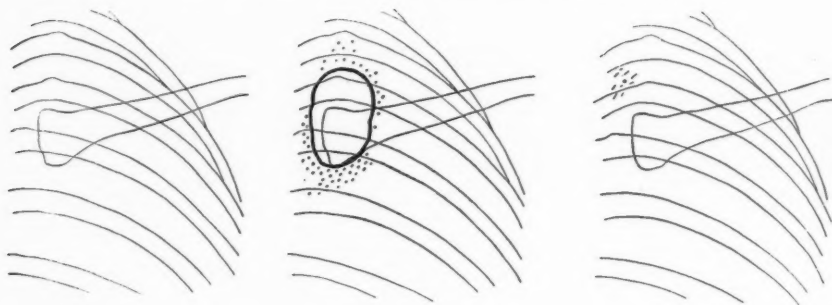
CASE 9.—(*a*) 25.2.52. F. 68 yrs. X-rayed as contact of Sp. + grand-daughter. X-ray clear.
(*b*) 3.12.52. Large cavity L. upper zone. Sp. +. Posture, L. side, 4 months. Chemotherapy: Strep. 42 gm. and P.A.S., followed by Strep. 2 gm. weekly plus I.N.A.H. for 10 weeks. (Total Strep. 62 gm.) Cavity closure in 3 months.
(*c*) 28.12.53. Patient well, leading normal life. X-ray reveals only a small node at site of cavity.

Theories differ as to the mode of action of this manœuvre. Surely the true explanation is that the procedure achieves the effect stipulated by Coryllos—namely, further relaxation of the diseased lung, with shortening, contraction and occlusion of the bronchi draining the cavities. Efficient posture also leads rapidly to complete cessation of cough.

Attention is drawn to the excellent results in bilateral upper zone excavation (case 5) and to the results in chronic disease of elderly people (cases 4 and 9).

Too frequently such cases are regarded as incurable, but as chronic carriers of tubercle bacilli, they are a grave risk to others.

Case 8 was a minimal lesion which, from other hands, may well have been handed to a surgeon for resection.

Most of the results shown were obtained with 12-inch blocks under the foot of the bed. It is felt that 15-inch blocks, as advocated by others, would be even more effective. For the first week raise the foot of the bed on 9-inch (23 cm.) blocks, for the second week on 12-inch (30·5 cm.) blocks, and subsequently on 15-inch (38 cm.) blocks.

Fourth Principle—Chemotherapy. The use of chemotherapy should be efficient and *limited*. The evolution of resistant organisms *must* be avoided. Patients must not be harmed in any way by possible toxic effects of the drugs used.

The M.R.C. (1953) in a recent report on chemotherapeutic trials stated that 1·5 per cent. of 432 cases submitted were excluded from the trials because of the presence of resistant organisms. During 1953, 16,495 new sputum-positive cases were reported in England and Wales. If 1·5 per cent. of these were expectorating resistant organisms (*i.e.*, a total of 250), the problem of resistance becomes one not only for the individual but for the community.

It has been the practice, in this work, to follow lines laid down by the M.R.C.

If results were good before the use of chemotherapy, how much better would they be if the advantages of chemotherapy were added to the existing régime.

Note, in the examples shown, the excellent results obtained with *limited* use of chemotherapy. Streptomycin was given in doses of 1 gm. daily, P.A.S. 16 gm. daily, and I.N.A.H. 100 mgm. twice daily.

Fifth Principle—Artificial relaxation therapy. In selected cases artificial relaxation therapy will assist in the prevention of relapse, and will frequently save the patient from drastic surgical intervention. Results, particularly with unilateral cavitation, have been so encouraging that fresh rules have been evolved for the use of artificial pneumothorax, which has become a much safer and more effective form of treatment following posture.

Rules for the use of artificial pneumothorax

(1) Artificial pneumothorax must not be used to close cavities.
(2) Cavity closure must first be secured before the induction of artificial pneumothorax.
(3) Following cavity closure artificial pneumothorax can be successfully used as a measure of *relaxation* during the patient's rehabilitation and return to work.
(4) When used as a means of relaxation following effective medical treatment, the artificial pneumothorax need not be maintained for a prolonged period.
(5) The use and management of artificial pneumothorax is a skilled procedure.

Examples of this technique are shown in cases 1, 2, 3, 6, 7. Note the short maintenance of refills in cases 3 and 7. When utilised in this way an artificial pneumothorax can often be abandoned, with safety, after eighteen months or so.

Discussion

Cavity closure can readily be obtained if there is the closest co-operation between physician and patient. Only a few examples, of many, can be shown here, but they are representative of differing types of disease and of age groups. Initially success was welcomed with pleasant surprise. Now it is anticipated. If striking improvement is not obtained after three months' postural rest, someone—physician or patient—is at fault.

The physician is at fault if he has not thoroughly instructed the patient in the nature of the disease, and in the measures which will lead to healing and recovery.

The patient is at fault if he is foolish enough to disregard the advice tendered. The striking results illustrated here have been obtained only with the full and willing co-operation of each patient.

CRUDE DEATH RATES OF PERSONS FROM TUBERCULOSIS AT ALL AGES TO A MILLION LIVING

TUBERCULOSIS - RESPIRATORY
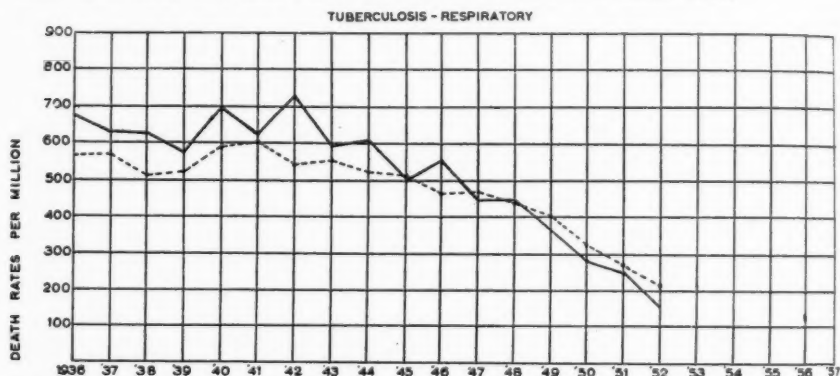
FIG. 2.—Dotted line—figures for England and Wales issued by Registrar-General. Solid line—figures for Willesden issued by Medical Officer of Health.

Many patients, who succumb to tuberculous disease, have been leading unhealthy lives, subject to mental and bodily harassment.

Patient No. 1 was an Irish contractor who admitted the consumption of a bottle of whisky and of sixty cigarettes daily. With full co-operation in his treatment he regained his health and working capacity.

Following recovery these patients are advised (1) never to smoke again and always to avoid coughing; (2) always to have regular meals with a daily amount of fruit and green vegetables; (3) to avoid becoming tired out by work or travel and to rest completely for half an hour on return home each evening. Compliance with these rules lessens fear of relapse.

In many instances success, after postural rest, may be consolidated by the induction and maintenance of some form of pulmonary relaxation (e.g., artificial pneumothorax or pneumoperitoneum), but the outcome depends more on the full co-operation of the patient than on any other factor.

Thoracic surgery undoubtedly has a part to play in the treatment of phthisis, but it should be regarded as an auxiliary to medical treatment and not

as *the* treatment of the disease. Before the help of the surgeon is enlisted, efficient medical treatment should aim at cavity closure. As in the new rules formulated for pneumothorax, thoracic surgery should be used to maintain pulmonary relaxation *after* cavity closure has been secured. With efficient medical treatment many patients need not undergo major surgical procedures (*e.g.*, resection or thoracoplasty). In many areas of Britain a bottle-neck is reported in the administration of this disease. Hundreds of patients are kept for prolonged periods in hospital or sanatorium beds awaiting thoracic surgery.

It is suggested that the wide adoption of these " principles of treatment " would alleviate this problem. Efficient treatment, as outlined here, is not costly. It does not need the erection of magnificent institutions or of expensive apparatus. It can be utilised freely both in this country and in other countries where facilities are poor or lacking.

Fig. 2 shows the effect of this policy on death rates from respiratory tuberculosis in Willesden, as compared with the recent record low rates in England and Wales.

Summary

The formation of tuberculous cavities is described.

The draining bronchus is all-important both in the evolution of a cavity and its closure.

The complete elimination of cough is vital for success in treatment.

A true understanding of these factors has led to the adoption of principles in the treatment of the disease.

Full co-operation of the patient is essential.

There is an art, as well as a science, in medicine. The art of successful treatment lies in the proper management of a human being—not an X-ray film.

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THE RE-EXPANSION OF THE LUNG AFTER EXTRAPLEURAL PNEUMOTHORAX

By Gianfranco Fegiz

From the Carlo Forlanini Institute, Tuberculosis Clinic of Rome University, Italy

Of the surgical methods now used for the treatment of pulmonary tuberculosis, thoracoplasty has a well-defined position, and its indications and results differ little in various countries. There is a certain body of agreement about the value of pulmonary resection, though the results so far obtained are *sub judice* and long-term results are still awaited. Extrapleural pneumothorax, however, though it has been practised for the past twenty years, remains a debatable form of treatment in different countries and schools. It is much in use in France and Italy, but it has never been popular in the Anglo-Saxon countries, Holland and elsewhere, and it continues to lose ground.

What are the reasons for the hostile attitude of some surgeons to this method, and how can one account for its employment on a large scale by others, who claim brilliant and lasting benefits from it?

This operation was first advocated by Omodei-Zorini in 1932, and it was carried out according to his technique. In 1936 Graf studied the problem, proposed different operative technique, and reported on his first cases. Since 1932 there have been over 1,000 extrapleurals performed at the Forlanini Institute. A full account of these was given by the Director, Professor Omodei-Zorini at the September 1954 Congress of Phthisiology in Madrid.

It must be admitted that for some conditions either thoracoplasty, extrapleural or resection, offers equally good chances of a successful outcome. The choice of operation generally depends on the special experience and temperament of the surgeon, and on the attitude of the patient. This seems the only plausible explanation for the noteworthy diversity of trends in the surgery of tuberculosis in various countries. But we feel that in the special case of the extrapleural, one of the main reasons for a certain unpopularity may result from the conviction that the lung collapsed by this method for several years is incapable of re-expansion, so that either a permanent collapse *ab initio* or a primary resection is preferred. Our experience in the early days was that re-expansion tended to occur prematurely within a few months, and it was precisely this difficulty which was overcome as a result of improved operative technique and better post-operative care.

Moreover, we feel that the procedure is essentially a reversible one, and should have as its final aim the re-expansion of the lung at the completion of treatment. In the series of Gernez-Rieux et al. (1943) and of Tapia et al. (1947) expansion was complete in a large majority of cases, and persistence of the space after abandonment was most infrequent in uncomplicated cases. De Bernart (1949) obtained good re-expansion in cases complicated by hæmothorax, and Valli (1948) in eighteen cases obtained successful re-expansion in fourteen. Le Foyer and Delbecq (1950), on the basis of their experience of

1,313 cases, stated that when the extrapleural was of good quality and had been applied on the basis of careful selection, re-expansion was generally complete; occasionally a fibrinous cap developed which, however, did not constitute any danger but, on the contrary, formed a sort of biological " plom-bage " over the apex of the upper lobe. These statements were generally confirmed by Berard (1954) at a lecture at the Forlanini Institute, in which the conclusions were based on a personal series of 1,300 cases. Our own experience of over 1,000 cases at the Institute repeatedly confirms that failure of re-expansion is uncommon.

The main reasons for failure of re-expansion can be classified as (1) bronchial, (2) pleural, and (3) parenchymal.

(1) In the presence of endo-bronchial disease the institution of *any* form of collapse therapy may produce a severe stenosis with resultant atelectasis. It is not therefore surprising that re-expansion cannot occur, and where this complication has resulted quite obviously there has been an error of selection.

(2) *Pleural thickening* may result from an old-standing hæmothorax, empyema or pleuro-pulmonary fistula. Here again the initial selection has generally been at fault, though assiduous treatment of the local condition by means of lavage, fibrinolytic substances and antibiotics may be successful; failure is generally the result of persistence of a fistula, which can only be treated by thoracoplasty or resection. Fistulæ are nowadays much rarer owing to adequate pre-operative treatment with antibiotics.

(3) *Parenchymal.* The selection of patients should be based upon the accurate assessment of the nature, extent and localisation of the disease process. In 1946-47, before the introduction of the newer methods of antibiotic and chemo-therapy, Omodei-Zorini on the basis of his classification of the types of lesions occurring in post-primary tuberculosis had enunciated those which were suitable for treatment by extrapleural pneumothorax. These have not been materially modified by the advent of antibiotic therapy, except in so far as the more acute types have been made operable more safely and earlier than previously would have been possible. The following classes of cases are regarded as suitable, and the indication for the operation *absolute*:

(a) Recent infiltration with early cavitation in the apical, subclavicular or subclavicular-juxta hilar areas, in which cavities are not more than 4 cm. in diameter, whose walls are not thin and in which there has been no bronchogenic dissemination throughout the rest of that lung.

(b) Recent infiltrations, with tendency towards clinical stabilisation, limited to a portion of the upper lobe, with numbers of small cavities.

(c) Micro-nodular or micro-cavitary tuberculosis of the apex, if there is not any undue fibrosis or pleural thickening.

(d) More diffuse forms, involving also the middle or lower third of the lung, of hæmatogenous type, in the breaking down stage, with the formation of small cavities.

The group of *relative* indications is to be found in recent lobitic and bronchopneumonic types, confined to the upper lobe; unilateral chronic diffuse miliary disease; isolated cavities of the upper lobe and of the parahilar region; and unilateral chronic phthisis of the mixed productive exudative type.

The use of antibiotics has shortened the necessary time before operation

can be undertaken, and we now generally operate two months after the inception of medical treatment, provided that the improvement is not such as to lead us to presume that recovery may occur without the necessity of operation. A further point which must be emphasised in regard to the question of expansibility is the manner of abandonment. As Omodei-Zorini says, this process must be " manipulated " very much as in the case of the intrapleural pneumothorax. Refills must be gradually diminished, with marked attention to the avoidance of high negative pressures, which tend to cause effusions. We do not regard the development of apical layers of fibrin as being a disadvantage, and would not agree that this constitutes a failure of the lung to expand.

On account of the diversity of our clinical material and because the indications for operation have continuously improved since 1942, it is not possible to furnish exact statistical data of the percentage of complications and re-expansions of the lung at the end of treatment, but we may claim that where the indications were correct and no pleural complications of importance developed, re-expansion of the lung was obtained without particular difficulty, and it has even been possible to effect medical or surgical collapse therapy on the opposite side.

The X-ray illustrations (Figs. 1-6) are of two typical cases selected from our vast clinical material, and they show unequivocally that the collapsed lung can re-expand after several years of treatment. Where the operation is indicated it should be carried out, since by reason of its action and reversibility it approaches the ideal of pulmonary rest which Forlanini enunciated and effected in introducing intrapleural pneumothorax.

Summary

The operation of extrapleural pneumothorax has gradually fallen into disrepute in some countries, whilst retaining its popularity in others. One of the reasons commonly given for its disrepute is the failure of re-expansion at the end of treatment; such failures should not occur when the case has been properly selected and the process of abandonment has been properly carried out.

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PLATE X

CASE 1

FIG. 1.—Isolated cavity of the right upper lobe with pleural symphysis (27.5.1947).

FIG. 2.—Same case: Extrapleural pneumothorax with tuberculous empyema (27.7.1947).
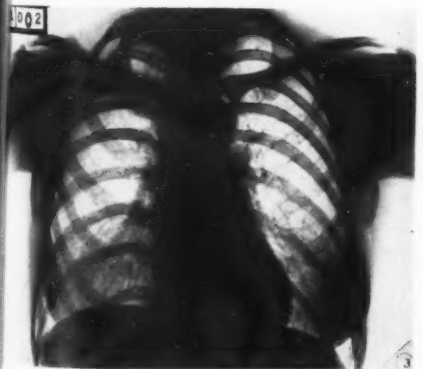
FIG. 3.—Same case: complete re-expansion of the lung after treatment of empyema and two and a half years of collapse.

CASE 2

FIG. 4.—Subclavicular cavity of the left lung with pleural symphysis (26.11.1946).

FIG. 5.—Same case during treatment with extrapleural pneumothorax (8.4.1947).
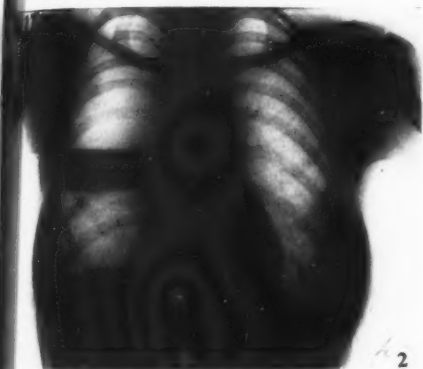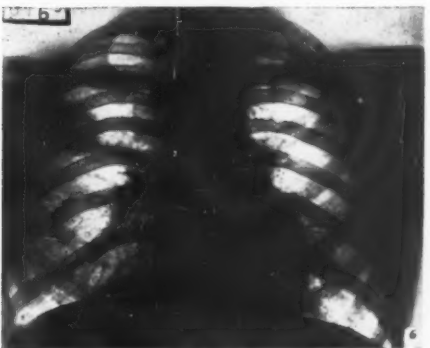

FIG. 6.—Same case after three years' treatment, controlled three years after last refilling. A cavity is present in contralateral lung (7.1.1954).

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BRONCHIAL TUBERCULOSIS

By W. Gordon

From St. George's Hospital, London

By studying the bronchi of lung tissue excised as treatment for pulmonary tuberculosis, Wilson (1945) correlated bronchoscopic and microscopic appearances and described three pathological stages of tuberculous bronchitis: (1) submucous infiltration, (2) ulceration and hyperplastic changes, (3) healing. These can coexist. They correspond with the common classification of bronchoscopic appearances—namely, (1) swelling of the mucous membrane of a degree sufficient to produce some narrowing of the bronchial lumen; (2) ulceration; (3) fibro-stenosis (Jarman, 1949; Keers, 1950; Richards, 1952). This classification does not include abnormalities due to compression or perforation of bronchi by tuberculous lymph nodes, but the latter may produce similar appearances (Morlock and Pinchin, 1933; Hutchison, 1949; Adler and Richards, 1953).

In the present investigation, bronchoscopy was performed on 100 hospital patients with pulmonary tuberculosis and an attempt made to correlate the bronchoscopic appearances with certain clinical and radiological features. All the recorded observations were made by the author. Twenty-four patients had received a short course of streptomycin from six months to three years before bronchoscopy and 76 had not been given antibiotic therapy.

Ulcers and fibrous strictures were not encountered. The only abnormality revealed was narrowing of the bronchial lumen by swollen and often red mucosa. Such mucosa showed evidence of tuberculosis in all of 7 cases in which the bronchi were examined histologically. When seen through the bronchoscope it was interpreted as evidence of bronchial tuberculosis.

Table 1 shows the reason for performing bronchoscopy and the incidence of abnormal appearances. The operations listed were not necessarily carried out at the time, as the bronchoscopic appearances sometimes led to postponement or alteration of the intended procedure. " Other " indications included bronchoscopies for unexplained positive sputum and to help in selecting the form of

TABLE 1.—BRONCHOSCOPIES ON 100 PATIENTS WITH PULMONARY TUBERCULOSIS

Indications for bronchoscopy						Total number of patients	With bronchial tuberculosis
Pre-pneumothorax	..	..	..	..	..	..	4	3
Pre-thoracoplasty	..	..	..	..	..	..	36	13
Pre-excision	..	..	..	..	..	..	37	22
Other	..	..	..	..	..	..	23	13
						100	51

treatment. Bronchial tuberculosis was present in 19 of 45 males and in 32 of 55 females, an overall incidence of 51 per cent.

In either sex the incidence of bronchial lesions was the same whether the pulmonary tuberculosis had been present for less than two years (average duration fourteen months) or more than two years (average duration nine years). The incidence of bronchial tuberculosis was the same whether the pulmonary disease was moderate or extensive on the X-ray film, but was higher with very extensive pulmonary disease. There were no patients with minimal pulmonary lesions.

Despite severe and long-standing disease in several patients, no abnormality of a main bronchus was seen. Elsewhere in the visible bronchial tree tuberculous lesions occurred on the right side as frequently as on the left, and the upper lobe bronchi were affected as often as the lower lobe bronchi. In some patients lesions were present at more than one site.

In Tables 2, 3 and 4 symptoms, signs and X-ray findings are correlated with bronchoscopic appearances in the 100 patients. Patients with severe cough, wheeze (rarely localised), and more than 2 oz. of sputum daily, are very likely to have bronchial tuberculosis. However, bronchial lesions were present in about half the patients with moderate, slight or no cough, or with less than 2 oz. of sputum daily, or without wheeze. Fifteen of these patients had a slight cough and scanty sputum only and 5 had no symptoms.

TABLE 2.—SYMPTOMS AND BRONCHOSCOPIC APPEARANCES IN 100 PATIENTS

Symptoms		Total number of patients	With bronchial tuberculosis
Cough	Absent	12	4
	Slight	60	26
	Moderate	18	12
	Severe	10	9
Sputum	None	13	4
	Trace	41	17
	Less than 2 oz.	29	16
	More than 2 oz.	17	14
Wheeze	Absent	91	44
	Present	9	7

TABLE 3.—PHYSICAL SIGNS AND BRONCHOSCOPIC APPEARANCES IN 100 PATIENTS

Physical signs	Total number of patients	With bronchial tuberculosis
Normal	42	15
Diminished movement	12	6
Diminished air entry	28	20
Tubular breathing	14	9
Rhonchi	11	9
Crepitations	15	8

TABLE 4.—X-RAY AND BRONCHOSCOPIC APPEARANCES IN 100 PATIENTS

X-ray appearances	Total number of patients	With bronchial tuberculosis
Collapse	29	24
Cavity with fluid level	9	9
Cavity persisting in anatomically perfect A.P.	2	2
Tension cavity (Not needled)	2	2
Cavity (no fluid level) or infiltration or both	53	13
Uncertain	5	1

In Table 3 the bronchoscopy reports and the physical signs concern the same parts of the lung. Diminished air entry and rhonchi are signs suggestive of bronchial tuberculosis, but the latter was present in 15 patients with no abnormal physical signs.

In Table 4 " uncertain " refers to X-ray appearances which were confused by some operative procedure such as a thoracoplasty. Significant X-ray appearances, such as collapse of lung tissue or cavity with a fluid level, were associated commonly with lesions in bronchi serving the abnormal parts.

BRONCHIAL LESIONS IN PATIENTS UNDERGOING THORACOPLASTY

Of 13 patients with normal bronchoscopies 12 did not have complications after thoracoplasty, but 1 suffered a spread of disease. Six patients had swollen, red mucosa in the upper lobe bronchus at the time thoracoplasty was performed; in 5 of these the operation was complicated by collapse of the lower lobe or spread of disease. Six other patients with swollen, red mucosa in the upper lobe bronchus were treated with parenteral streptomycin 1 gramme daily. After eight weeks of this therapy the bronchoscopic appearances were greatly improved in 2 and normal in 4. These patients then underwent thoracoplasty without complications.

Discussion

In the present investigation, most of the patients had the same clinical features whether they had bronchial tuberculosis or not. On the other hand, certain symptoms, signs and X-ray appearances were practically confined to patients with bronchial disease. These were severe cough, more than 2 oz. of sputum daily, wheeze, diminished air entry, rhonchi, collapse of lung tissue and cavity with a fluid level. Table 5 shows the number of patients with each of these features and the number of these patients with bronchial tuberculosis. None of the symptoms, signs or X-ray appearances was present in more than 29 per cent. of the patients, but of those patients with any one of these clinical features bronchial tuberculosis was seen in not less than 71 per cent. Thus it appears that these symptoms and signs are reliable guides to the presence of tuberculosis of the larger bronchi. However, as the disease exists frequently in the absence of such characteristics, bronchoscopy is needed to confirm the suspected diagnosis and to determine the distribution and severity of the lesions.

Lesions were seen at bronchoscopy in 51 of 100 patients with pulmonary

TABLE 5.—SYMPTOMS, SIGNS AND X-RAY APPEARANCES COMMONLY ASSOCIATED
WITH BRONCHIAL TUBERCULOSIS

Clinical feature						Total number of patients	With bronchial tuberculosis
Severe cough	..	..	..	..	..	10	9 (90%)
More than 2 oz. of sputum daily	..	..	..	..		17	14 (82%)
Wheeze (rarely localised)	..	..	..	..	..	9	7 (78%)
Diminished air entry	..	..	..	..	..	28	20 (71%)
Rhonchi	..	..	..	..	..	11	9 (82%)
Collapse of lung tissue	..	..	..	..	..	29	24 (83%)
Cavity with fluid level	..	..	..	..	..	9	9 (100%)

tuberculosis; but this probably does not represent the incidence of tuberculosis in their major bronchi. The British Tuberculosis Association (1953) reported that in 94·6 per cent. of 56 cases with normal bronchoscopic appearances, histological evidence of endo-bronchial disease was obtained. In the present series such evidence was found in 20 of 24 patients with normal bronchoscopic appearances. When a bronchus is to be transected, as in pulmonary excision, the microscopical lesions have a special significance and require pre-operative treatment whether bronchoscopy is abnormal or not (Gordon, 1954). No doubt tuberculous lesions of the bronchi are very common in patients undergoing thoracoplasty, but they appear to be dangerous only when they cause gross changes visible at bronchoscopy. It is suggested that these be treated with parenteral streptomycin before operation to diminish the incidence of post-operative complications.

Summary

1. Bronchoscopic and certain clinical features are recorded in 100 patients with pulmonary tuberculosis. Bronchial tuberculosis was seen in 51.

2. The value of clinical features in the diagnosis of bronchial tuberculosis is discussed.

3. The incidence of macroscopical and microscopical disease is compared and the relationship between bronchial lesions and certain complications following thoracoplasty is discussed.

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THE BLOOD SEDIMENTATION RATE AND FRACTIONAL PLASMA VISCOSITY IN PULMONARY TUBERCULOSIS

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Introduction

It has long been felt that changes in the blood may give a useful indication of the extent of tissue damage in disease. Since the time of Galen the buffy coat, an effect depending on the sedimentation rate, has been recognised and indeed formed an important part of the humoral theory. In 1877 Biernacki studied the sedimentation rate as such and recognised its relationship with the fibrin content; but it was not until 1920, when Linzenmeier and Westergren independently produced methods of estimating the sedimentation rate using small amounts of blood, that this test was widely adopted in clinical practice. The extensive investigations of Fahreus in 1921 confirmed the importance of fibrinogen and established the role of the remaining plasma proteins in the mechanism of rouleaux-formation and the sedimentation of red blood cells. Subsequently, when the very serious fallacies connected with the test came to be recognised, attempts were made to overcome these by more direct methods of studying the plasma proteins. Daranyi (1922) evolved a test for estimating colloid lability of the serum as tested by alcohol precipitation of the serum proteins, and claimed that this gave a more accurate indication of the activity of disease than the erythrocyte sedimentation rate (E.S.R.). Other tests of colloid lability followed (Frisch and Starlinger, 1922; Matéfy, 1923), including the formol gel and antimony tests, which also serve to indicate an increase of the more labile globulins.

In 1930 Weltmann introduced his coagulation test by which he attempted to differentiate between exudative and proliferative disease. Recent analyses indicate that this depends on increase of α and γ globulin respectively in the patient's serum.

During the middle thirties interest centred mainly on the leucocyte changes, particularly the ratio of lymphocytes, monocytes and polymorphs as expressed in the Crawford-Medlar index (Crawford, 1935) and the incorporation of the latter with the Bonsdorff count and the E.S.R. in the Houghton index (Houghton, 1935). These tests were, however, concerned more with prognosis and with the reaction of the patient to his infection and no attempt was made to correlate them with the activity of the disease process. They are indeed now little used and only the blood sedimentation rate is commonly employed.

Electrophoretic studies have been made by a number of workers. Baldwin and Iland (1953) have shown that α^1, α^2 and γ globulin are increased in

active pulmonary tuberculosis with a corresponding decrease in albumin. In the samples examined by these workers β globulin was not always increased and sometimes showed a slight decrease in severely ill patients. Volk and his colleagues (1953) found the γ globulin increased in all moderately advanced and severe disease, and in the two patients with minimal disease whom they studied. In cases which clinically appeared to be arrested the γ globulin was generally within normal limits. The α^2 and β globulins, on the other hand, sometimes remained raised after clinical arrest of the disease.

The plasma viscosity was first studied in relation to pulmonary tuberculosis in 1940 by T'ang and Wang, who found it a more sensitive test of " activity" than the E.S.R. In 1942 Miller and Whittington independently reached a similar conclusion and this was later confirmed on a large series by Houston, Whittington, Cowan and Harkness (1949).

The test was subsequently extended to include a study of the viscosity of the plasma during fractionation of the proteins (Lawrence, 1949, 1950), and this in turn appeared to give a still more accurate assessment of disease activity in a wide variety of pathological states.

MODES OF ASSESSMENT

In his study of the E.S.R. in pulmonary tuberculosis Westergren used prognosis as assessed by mortality in a subsequent follow-up. This has the advantage that the basis of assessment is entirely factual; it is, however, not essentially a measure of disease activity at the time of the test.

Miller and Whittington used the National Classification as a means of comparison. They concluded that there was a close association between this grouping and the plasma viscosity.

In this investigation on patients undergoing treatment in the Crossley Hospital, the blood changes have been compared with the following aspects of the disease process.

(1) A clinical assessment.
(2) A radiological assessment of both the extent of the disease and its progress.

The clinical assessment of activity presents considerable difficulty, depending as it does on eliciting and correlating divers signs and symptoms. It follows that where such an assessment is used to determine the relative value of laboratory tests it may be difficult to exclude an element of personal bias. In an attempt to minimise this bias in the present study, the assessment of clinical activity and radiological change was made by one of us (J.H.) without knowledge of the blood changes, and the relationship was then examined.

SELECTION OF PATIENTS

For assessing the activity and extent of the disease respectively, different methods of sampling are required. To assess the relationship of activity to blood changes it is desirable that the extent of the disease should be kept as constant as possible and therefore a large number of tests should be made on a few patients. To assess the extent of the disease in relation to blood changes, on the other hand, the clinical activity should be as constant as possible and

only one test should be included from each patient, preferably before active treatment has been started.

For the clinical assessment we have taken 250 samples of blood, many from the same patient at different stages in the progress of the disease. Of these samples 50 were taken during the active febrile stage, 50 when the disease was active but afebrile, 50 at a stage when activity was doubtful, 50 when the disease was considered as possibly inactive, and 50 when it was definitely inactive. A temperature of 99° F. was taken as the cutting point between the febrile and afebrile patients.

For the purpose of the radiological study 100 consecutive patients were chosen and the first complete test on each was used. In this way a representative cross-section of all patients admitted to the hospital was assured and all grades of radiological involvement were included.

Patients having complications such as empyema or hæmothorax or who showed evidence of any other disorder—e.g., rheumatoid arthritis—likely to affect the plasma proteins, were excluded. Non-purulent pleural effusions associated with demonstrable intra-pulmonary disease were included.

The technique used for the total and fractional viscosities has been described elsewhere (Lawrence, 1950). The E.S.R. was estimated by the Westergren method, but carried out at 37° C. and read after thirty minutes. This gives results almost identical with those obtained after one hour at 18° C. and avoids error due to variation in room temperature or to the presence of cold agglutinins.

Results

Comparison with clinical assessment of activity. With all tests a higher proportion of abnormal values was found in the active febrile than in the active afebrile patients (Table 1). Two of the tests (globulin 2 and albumin) showed no other significant features and will not be discussed further. The remaining four tests all proved capable of distinguishing active cases, whether febrile or afebrile, from those who were inactive or of doubtful activity. Indeed, the differences between active and doubtfully active patients were in all instances statistically significant. No significant differences were found in any of the tests between those of doubtful activity and those who were definitely inactive, but in the case of globulin 1 there was a progressively increasing number of abnormal values with each step in the grading, and it would appear, therefore, that globulin 1 gives the most reliable information on this score.* From this point of view it is important to consider in what proportion of active cases each of these tests is of value. Thus the E.S.R. is raised in only 36 per cent. of definitely active cases, whereas the total viscosity is abnormal in 63 per cent., fibrinogen in 50 per cent. and globulin 1 in 68 per cent. Statistically each of these viscosity tests is significantly more effective in this respect than the E.S.R. As the total viscosity is almost as reliable as the globulin 1 viscosity it is worth considering whether the total viscosity alone is sufficient or whether the fractions should be added. In column 7 of the table an assessment is given of the proportion of samples in which the total or one

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* Globulin 1 may be taken as indicating changes in the γ globulin. Globulin 2 is related to α globulin.

TABLE I.—RELATIONSHIP OF CLINICAL ASSESSMENT OF ACTIVITY TO BLOOD CHANGES

Clinical assessment	E.S.R.	Number of results beyond normal levels						Total viscosity or one of the fractions	E.S.R. or total or fractional viscosity	Total samples
		Plasma viscosity								
		Total	Fibrinogen	Globulin 1	Globulin 2	Albumin				
Active and febrile ..	22 (44%)	35 (70%)	30 (60%)	36 (72%)	9 (18%)	7 (14%)	44 (88%)	45 (90%)	50
Active and afebrile ..	14 (28%)	28 (56%)	20 (40%)	32 (64%)	4 (8%)	0 (0%)	38 (76%)	38 (76%)	50
? Active	4 (8%)	17 (34%)	6 (12%)	21 (42%)	6 (12%)	3 (6%)	28 (56%)	30 (60%)	50
? Inactive	6 (12%)	10 (20%)	10 (20%)	16 (32%)	1 (2%)	2 (4%)	21 (42%)	21 (42%)	50
Inactive	4 (8%)	12 (24%)	7 (14%)	13 (26%)	5 (10%)	2 (4%)	24 (48%)	26 (52%)	50

of the fractional viscosities alone or together is abnormal. Into this category 82 per cent. of definitely active cases fall. When the E.S.R. is added as shown in column 8 the figure rises to 83 per cent. There is thus a clear advantage in carrying out both a total and fractional viscosity examination, but it is doubtful whether the E.S.R. warrants even the small extra time involved.

The relationship of the clinical assessment to the average values for the E.S.R. and plasma viscosity are shown graphically in Fig. 1. This is chiefly
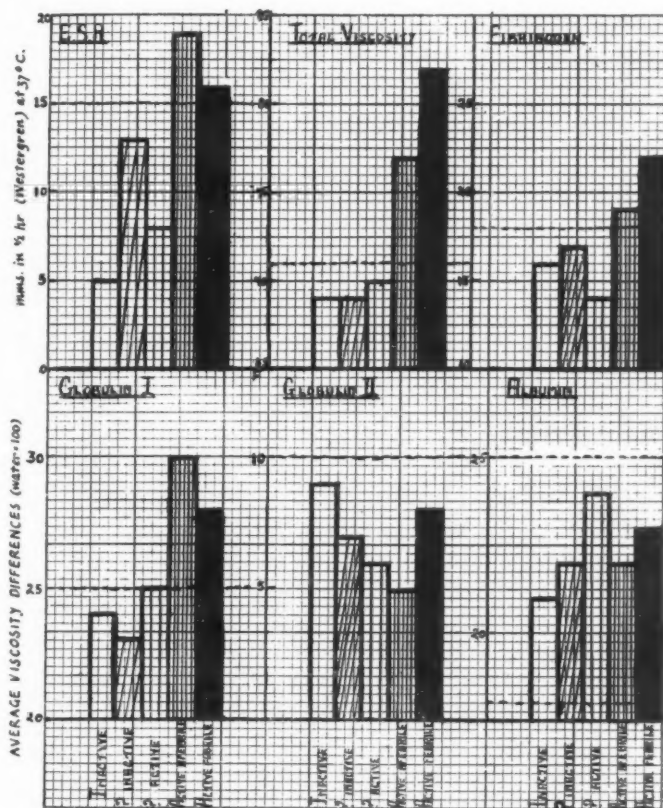
FIG. 1.—RELATIONSHIP OF CLINICAL ACTIVITY TO E.S.R. AND PLASMA VISCOSITY.

of value for comparison with the figures which appear later, but shows the fairly close relationship between the plasma viscosity and clinical activity.

Comparison with extent of disease. The extent of lung involvement was assessed from the radiographic appearance without a knowledge of the laboratory findings. Each lung was assessed separately, the diseased area being expressed roughly as a proportion of the whole lung. The average for both lungs was used for the preparation of the graphs.

In Fig. 2 comparison is made between the extent of lung involvement on
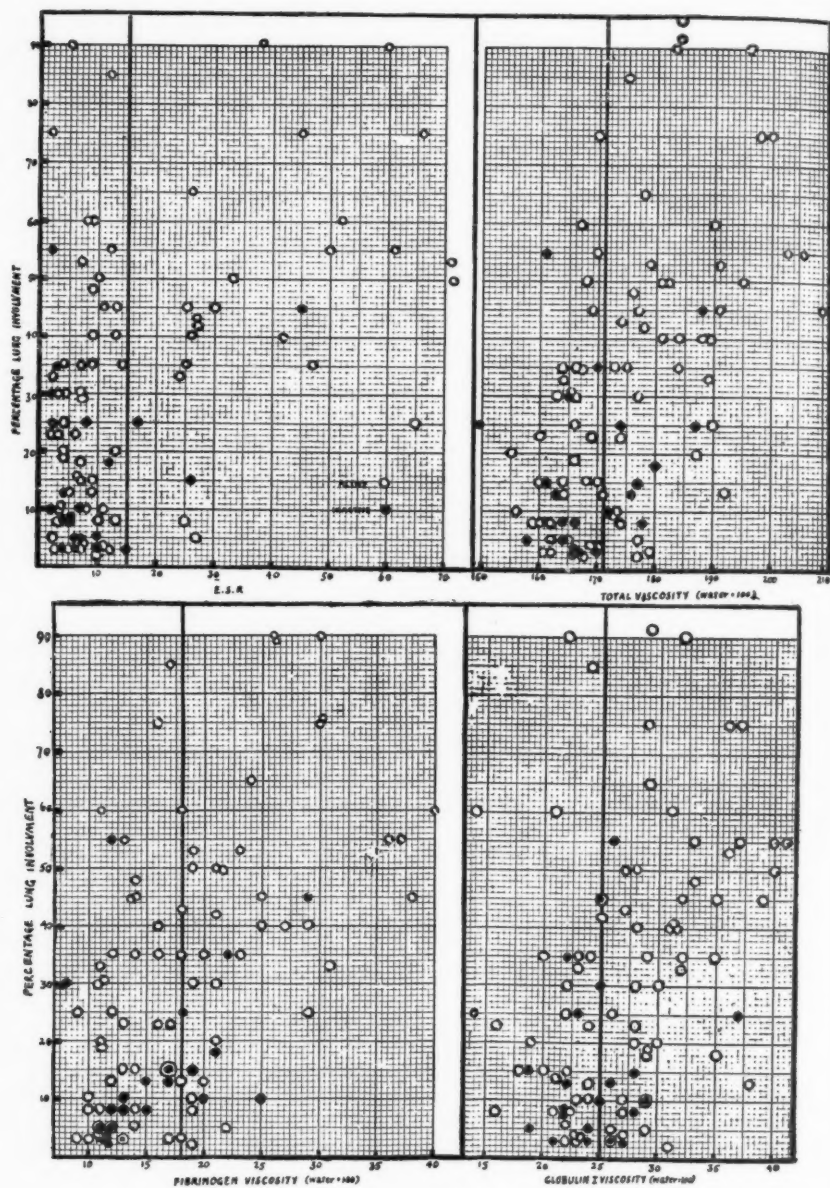
FIG. 2.—RELATIONSHIP OF EXTENT OF DISEASE TO E.S.R. TOTAL VISCOSITY, FIBRINOGEN, AND GLOBULIN I.

the one hand and the E.S.R., total viscosity, fibrinogen and the first globulin fraction on the other. The second globulin and albumin fractions were so seldom abnormal that it was felt they offered no useful contribution. In this diagram those considered clinically active are represented by circles, the inactive by dots.

It will be understood that, in view of the marked variation in the degree of activity between patients, no precise correlation with the extent of lung involvement can be expected. Clearly the involved area of lung may include both active and inactive zones, and an assessment of this type must include
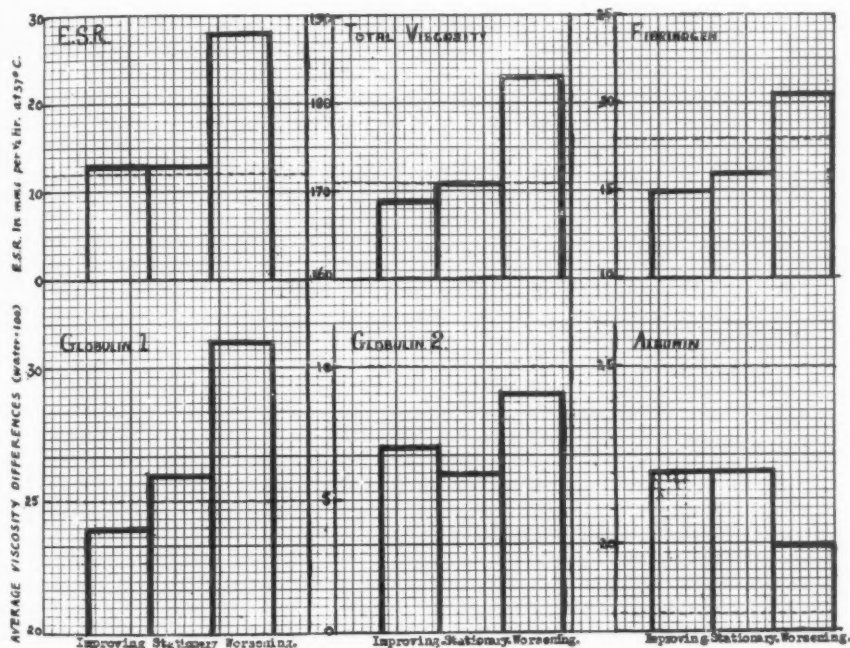
FIG. 3.—RADIOLOGICAL VARIATION.

all grades without regard to any possible effect which activity may have on plasma protein changes.

Nevertheless a certain trend can be recognised, particularly in regard to globulin 1 and the total viscosity, those with more extensive disease tending to have a higher viscosity value. This trend is less marked for fibrinogen, and still less for the E.S.R. which shows a large proportion within normal limits. The indications are, therefore, that the plasma proteins, particularly globulin 1, are influenced by the extent of the disease in addition to the degree of activity.

Comparison with Radiological Variation. Assessment of radiological variations was made on the same group of patients by comparison of the X-ray taken at or near the time of the test with that taken two months previously. In this

way a useful indication of recent progress was obtained. It was recorded as " improving," " stationary " or " worse."

Fig. 3 expresses the results diagrammatically, and is based on average results for each of the three groups. The most satisfactory correlation is again shown by globulin 1, but the total viscosity and fibrinogen also show a progressive increase with radiological deterioration. The E.S.R. is on the average higher in those in whom the X-ray is worse, but does not reflect radiological improvement. Albumin, although the average results are all within normal limits, shows a reduction in the deteriorating group. Globulin 2 does not reflect the changes in the X-ray picture.

In addition comparison was made with the temperature. Only the E.S.R. was closely related, though there was some relationship with the fibrinogen and with globulin 2.

Discussion

Until the mechanism of plasma protein control and of its response to tissue katabolism is known it is impossible to explain fully the changes in disease or to understand their significance as a measure of tissue change. Nevertheless it is clear that certain variations in the plasma protein levels take place when disease is in an active phase and that there is a return to normal with recovery. It would appear justifiable therefore to assume that these changes provide a measure of the activity of the disease process and to use them as an aid to clinical and X-ray evaluation in the control of treatment.

In the past the only method in general use has been the E.S.R., but it has been realised for some time, particularly by clinicians dealing with pulmonary disease, that the value of this test is very limited and indeed many have abandoned it altogether. That the E.S.R. should be an unreliable guide is not surprising when it is considered that the rate of sedimentation is mainly influenced by the fibrinogen content of the plasma (Fahreus, 1921) with secondary effects from α^2 globulin and very little from β or γ globulin (Gray and Mitchell, 1942; Hardwicke and Squire, 1952). Our figures and those of Baldwin and Iland (1953) have shown, however, that it is the γ globulin which is chiefly affected in active pulmonary tuberculosis and that the fibrinogen and the other globulin fractions are less constantly disturbed and indeed are often within normal limits. Moreover, in pulmonary tuberculosis, as in other lung disease where there is deficient oxygenation of the blood, there is sometimes a relatively high ration of red cells to plasma. It has been shown in a previous paper (Lawrence, 1953) that even a slight increase of the cell-plasma ratio has a profound effect on the E.S.R. It would not be surprising, therefore, on theoretical grounds if the E.S.R. proved unreliable, and this is well shown by our findings of an abnormal result in only 36 per cent. of definitely active cases.

The plasma viscosity, on the other hand, is independent of the cell-plasma ratio and is greatly influenced by the γ globulin content of the plasma. The following shows the proportion which each protein fraction subscribes to the total in an average sample of plasma:

		Per cent.
Albumin	.. .. ..	36
Globulin 1 (γ)	.. ..	31
Fibrinogen	.. ..	22
Globulin 2 ($a+\beta$)	..	11

As the albumin fraction is never increased, except in extreme dehydration, the γ globulin variation is likely to be the main factor. Indeed our results show that as a reflection of clinical activity the total viscosity is almost as useful as the γ globulin viscosity-difference alone. As, however, any fraction may contribute to the assessment, a simple total viscosity estimation is not advised. A simple total viscosity is, however, much superior to the E.S.R. and should certainly be used if the full fractional viscosity cannot be carried out. As an additional test to the fractional viscosity the E.S.R. in pulmonary tuberculosis is scarcely worth while, as it only increases the accuracy by 1 per cent. This, however, does not necessarily apply in diseases other than tuberculosis, and particularly in non-pulmonary disease where the cell-plasma ration is less often raised and in which the γ globulin is often much less affected than for example the fibrinogen or a globulin. In Table II the proportion of abnormal results in pulmonary tuberculosis and other conditions in general are compared, and it is shown that in the latter the E.S.R. is of relatively greater importance, particularly in conjunction with the fractional viscosity technique.

TABLE II.—PROPORTION OF ABNORMAL VALUES IN PATIENTS WITH CLINICALLY ACTIVE DISEASE

	Pulmonary tuberculosis		*Disease in general*	
Total	100		245	
E.S.R. raised	36	36%	130	43%
Total plasma viscosity raised	63	63%	145	59%
Total plasma viscosity or one fraction raised	82	82%	212	86%
E.S.R. or total plasma viscosity or one fraction raised..	83	83%	231	94%

It should be pointed out that the γ globulin and fibrinogen are reduced following hæmorrhage and that the globulin may take several weeks to return its previous level. A raised level may thus be obscured after a severe hæmoptysis and this must be borne in mind when interpreting viscosity figures.

Summary

(1) The E.S.R. and the total and fractional viscosities of the plasma have been compared with a clinical and radiological assessment in a group of patients with pulmonary tuberculosis.

(2) The E.S.R. was found to be raised only in 36 per cent of the clinically active cases, the fibrinogen in 50 per cent., the total viscosity in 63 per cent. and the γ globulin in 68 per cent. The remaining fractions proved less helpful. The total and fractional viscosities taken together showed an abnormality in 82 per cent., but the addition of the E.S.R. gave only a further 1 per cent. improvement.

(3) The radiological extent of the disease influenced the plasma proteins in the same way, the γ globulin showing most response, and the E.S.R. was little affected.

(4) Radiological improvement was reflected in the plasma proteins and E.S.R. in the same way as the clinical assessment.

(5) It is concluded that plasma viscosity gives a useful indication of the activity in pulmonary tuberculosis, especially if the fractional technique is used. The E.S.R. would appear to be of little assistance.

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PROLONGED PULMONARY EOSINOPHILIA

A REPORT ON THREE CASES

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THERE have been many studies on the classification of pulmonary eosinophilia, Grayce (1946) suggesting that it included a number of conditions of varying severity with the transient Löffler's syndrome at one end of the scale and poly-arteritis at the other.

The whole subject has been thoroughly discussed by Crofton, Livingstone, Oswald and Roberts (1952), and they divided the intervening cases into prolonged pulmonary eosinophilia, with or without asthma, and tropical eosinophilia. They reported twelve cases of the prolonged type, seen by them in hospital practice in the course of the previous few years.

The purpose of this paper is to report three such cases of prolonged pulmonary eosinophilia known to have occurred during the past four years in the district, with a population of about 150,000, served by the Bedford General Hospital, and to report the use of A.C.T.H. in one patient.

CASE I.—A male journalist, aged 30 years, was seen at the Bedford Chest Clinic on January 9, 1950, with the following history. From the age of three to five years, he suffered from attacks of bronchial asthma; these recurred for a short period when he was sixteen.

He developed acute bronchitic attacks during 1948 which recurred every few months for the next two years, during which time he lost two stones in weight.

In August 1948 a radiograph had shown patchy opacities in both upper and mid-zones, and in April 1949 a further film showed a fresh opacity in the right mid-zone, the others having largely cleared. At this time he had slight pyrexia, purulent sputum, an E.S.R. of 30 mm. per hour, a normal blood count and six sputum specimens negative for tubercle bacilli.

In December 1949 he developed an acute respiratory illness accompanied by fever, lassitude and blood-stained sputum. He was investigated in hospital, where a radiograph on January 12 showed patchy shadowing throughout the upper half of the left lung with coalescence in the mid-zone, there being only linear markings in the right lung; another, six days later, showed considerable clearing with a fresh opacity below the right clavicle.

Repeated sputum specimens were negative for tubercle bacilli on culture. A new shadow below the right clavicle appeared on a film on February 6, and by June he had no symptoms, but a film showed a new opacity in the second right space. In September his peripheral blood contained 1,260 eosinophils per c.mm. (14 per cent. of 9,000 W.B.C.).

A bronchogram was performed and abnormality was demonstrated in the anterior and apical segmental bronchi of the right upper lobe (the posterior

not being filled), in the anterior basal and dorsal of the lower lobe, in the apical, anterior and lingula bronchi of the left upper lobe, and in the lateral basal and dorsal of the lower lobe. The character of the abnormality was not usual and will be discussed later.

Since then, several acute episodes have occurred and his latest radiograph shows extensive bilateral pulmonary fibrotic changes with a fresh opacity in the right lower zone; the peripheral blood contains 1,620 eosinophils per c.mm. (10 per cent. of 16,200 W.B.C.).

CASE II.—A school matron, aged 49 years, was seen on November 7, 1950, with a year's history of cough productive of mucoid sputum, some loss of weight and exertional dyspnœa. There was a previous history of pneumonia first at the age of five and again in October 1950. There was no allergic or tuberculous family history. A radiograph showed an ill-defined opacity in the right lower zone with a central ring shadow 1 cm. diameter. A compact shadow ran outwards from the cardiac border into the fourth left interspace. Sputum was negative for tubercle bacilli on repeated examination, blood count was normal, E.S.R. 4 mm. per hour and Mantoux positive to 1/1,000 O.T.

The signs and symptoms improved for a while, but in December a radiograph showed consolidation and collapse in the right upper lobe, mainly anterior segment, while the lingula and right base cleared. Peripheral eosinophils numbered 1,224 per c.mm. (12 per cent. of 10,200 W.B.C.). A further film, on January 9, 1951, showed extension of the opacity in the right upper zone and she was admitted to hospital. Her only symptoms were considerable lassitude and slight irritative cough. Her sputum contained *Staph. albus* with a few colonies of pneumococci and *N. catarrhalis* on culture, all sensitive to penicillin. No ova were found in her stools and urinalysis was normal. Treatment with physiotherapy and penicillin was instituted with considerable clearing of the shadow. By February, on discharge, her count was 980 eosinophils per c.mm. (14 per cent. of 7,000 W.B.C.). In March she had a consolidation of the right lower lobe accompanied by fluid. She was readmitted to hospital, where no abnormal organism or fungus could be found in her sputum, agglutination tests of Q fever, Streptococcus M.G. and cold agglutinations were all negative, as was the W.R. No ova could be found in her stools. Treatment with Penicillin, Chloramphenicol and Anthisan failed to relieve her symptoms, which consisted of a productive cough, lassitude and some emotional disturbance.

She was discharged in June with a count of 296 eosinophils per c.mm. (4 per cent. of 7,400 W.B.C.), and continued well except for an attack of jaundice in March 1952, at which time her count was 742 per c.mm. (7 per cent. of 10,600 W.B.C.) and the sputum contained 400 eosinophils per c.mm. Clearing of shadows at the right lung base continued slowly, but her count remained elevated, 576 eosinophils per c.mm. in August (6 per cent. of 9,600 W.B.C.), and in December 1952 a bronchogram was performed which showed a normal left lung but cylindrical bronchiectasis of the usual type involving the middle lobe bronchi and all the basal branches of the right lower lobe. She remained well during 1953 with normal counts throughout the year, except for one flare-up which settled with penicillin, but in January 1954 she had a fresh shadow in the lingula with 742 eosinophils per c.mm. (7 per cent. of 10,600 W.B.C.). This cleared slowly and the count dropped to normal by April but had risen again by August to 780 eosinophils per c.mm. (10 per cent. of 7,800 W.B.C.).

CASE III.—A housewife aged 50 years, under the care of Dr. J. Rutherford Tree, complained in May 1953 of the onset of lassitude and chronic nasal catarrh which continued with the addition of irritating cough. In July she underwent antral puncture with considerable improvement.

On September 11 a chest radiograph was normal but cough and lassitude persisted. A blood count was normal. In October, dyspnœa developed and she was found to have developed signs of a left pleural effusion. A radiograph on November 6 showed nodular shadowing in both lungs with coalescence at both apices, particularly the left, also a left effusion. Her sputum contained no tubercle bacilli or malignant cells. Her peripheral blood contained 460 eosinophils per c.mm. (5 per cent. of 9,200 W.B.C.) and the pleural fluid contained many eosinophils. No improvement was effected by the administration of Aureomycin and two injections of N.A.B. By November 24 the blood count was up to 3,300 eosinophils per c.mm. (25 per cent of 13,200 W.B.C.). Serum electrophoresis indicated a rise in the gamma globulin. A small right pleural effusion developed and then both were absorbed. In view of increasing loss of weight, fever up to 102° F. (39° C.), deteriorating general condition and an X-ray picture very suggestive of tuberculosis, she was admitted on December 28 to the Brompton Hospital under the care of Dr. F. P. Lee Lander. She was very ill and a radiograph showed patchy consolidation in the left mid and upper zones, also a hazy opacity in the right upper zone with infiltrative shadows extending down the mid-zone. Her blood contained 4,716 eosinophils per c.mm. (18 per cent. of 26,200 W.B.C.). Her urine and stools were normal.

Bronchoscopy showed no abnormality and on January 14, 1954, a formal thoracotomy was performed. The left upper lobe and apex of lower lobe were studded with fleshy nodules, varying from ½ cm. to 4 cm. in diameter, becoming confluent posteriorly.

The histological report on a biopsy specimen was as follows: " Section of this material shows the nodule is a granuloma in which there are a large number of eosinophils. There is considerable fibroblastic activity both in the interstitial tissue and in the alveoli. There is marked vascular degeneration present but no unduly acute periarteritis has been seen in the section. The appearances are those of an eosinophilic granuloma."

On January 21 treatment with A.C.T.H. 45 units q.d.s. was commenced. Dosage was gradually reduced and the drug changed to A.C.T.H. Gel. By February 3 the dose was 20 units daily and it was finally discontinued on February 17. Response to A.C.T.H. was dramatic, the temperature falling to normal within twenty-four hours while her symptoms took very little longer to clear. Radiological improvement was also noted within twenty-four hours, and by the end of the four weeks' course the only abnormality was residual basal pleural thickening. Thirteen eosinophils per c.mm. (17,000 W.B.C.) were present in the blood on the sixth and 31 per c.mm. (17,000 W.B.C.) on the nineteenth day of treatment. The day after treatment was terminated, however, the count was 706 eosinophils per c.mm. (9 per cent. of 7,840 W.B.C.), at which time she was discharged home. She kept well for a short time, but by the end of March her count had risen to 2,100 eosinophils per c.mm. (21 per cent. of 10,000 W.B.C.) and a week later to 2,142 eosinophils per c.mm. (7 per cent. of 30,600 W.B.C.), and she was restarted on A.C.T.H. Gel 25 units b.d. for three days and thereafter once daily for two weeks. On May 3 her count was 1,664 eosinophils per c.mm. (16 per cent of 10,400 W.B.C.) and a radiograph showed fresh mottling at both apices. Administration of 25 units of A.C.T.H. Gel daily was resumed and gradually reduced to 10 units daily.

In June her count was 504 eosinophils per c.mm. (4 per cent of 12,600 W.B.C.) and she felt very well and full of energy while the chest radiograph was normal again. By July, however, her count was up again to 1,176 eosinophils per c.mm. (14 per cent. of 8,400 W.B.C.) while her general condition had deteriorated. The dosage was raised 20 units daily with a drop in the count by August to 490 eosinophils per c.mm. (5 per cent. of 9,800 W.B.C.) and improvement in well-being.

She continues on this dosage and her most recent radiograph in September is clear, while her blood contains 588 eosinophils per c.mm. (6 per cent. of 9,800 W.B.C.).

Discussion

It is not possible to assess the incidence of prolonged pulmonary eosinophilia in this country, as few cases have been reported. As three patients suffering from this illness have been found in the course of four years in a fairly small population, it is probably more common than is realised. Few cases of the prolonged type without asthma have been reported in this country, and Cases II and III fall into this group, showing the usual features with migrating pulmonary shadows, the development of new areas of involvement usually being associated with constitutional upset. The course of Case II has been, to date, a low-grade four years' illness with periodic exacerbations, while that of Case III has been much more tempestuous. In neither case was there any personal or family allergic history nor evidence of polyarteritis nodosa. Case I falls into the more common group of eosinophilia with asthma, although it is noted that the degree of eosinophilia in all three cases is less than usually reported.

An interesting feature in two of these cases is the presence of bronchiectasis. Crofton et al. (1952) mention this and several of their cases of prolonged eosinophilia showed bronchial dilatation. Case I shows extensive ectatic abnormality covering all the areas in which infiltration is known to have occurred, but the character of the abnormality is unusual in several of the bronchi affected, as these show saccular dilatations in part of their course, continuing with normal contour thereafter to the periphery. Alveolar filling beyond many of these abnormal bronchi is normal. These abnormalities were described by Livingstone (1950).

It is generally agreed that recurrent pneumonic consolidations occur in many bronchiectatic patients, and that these usually occur in the ectatic segments. In Case II it is possible, in view of the history, that she had bronchiectasis before the development of pulmonary eosinophilia, but she had no bronchiectasis in the left lung or right upper lobe while infiltrations appeared in these areas.

The differences of this type of bronchial abnormality suggest the possibility that the bronchiectasis succeeds and does not precede the areas of infiltration in at least some cases, and the fact that ectatic bronchi are found so commonly in the upper lobes of these patients also points to a difference from the common form of bronchiectasis. It is very probable, in view of necropsy reports and the work of Samter et al. (1953), that the peribronchial tissue is the seat of the production of an eosinotactic substance following an antigen/antibody reaction.

Infection is not apparently a factor and an arteritis of varying severity is a

feature of the condition. As the peribronchial vessels are affected this may well lead to damage of the bronchial wall and, as a result, bronchiectasis.

Several reports have been published abroad giving details of the response of pulmonary eosinophilia to adrenocorticotropic hormone. Essellier and Koszewski (1951) and Mattson (1952) report on its action in Löffler's syndrome, while Andrell *et al.* (1949), Rose (1950) Vines and Clark (1951), Hantschmann (1952), and Reeder and Goodrich (1952) all report cases of prolonged pulmonary eosinophilia, mostly with asthma, responding in dramatic fashion to A.C.T.H. or cortisone, Schwartz (1952).

The pattern of response to A.C.T.H. in Case III with dramatic initial change followed by relapse if the drug be withdrawn confirms the association between this condition and collagen disease.

Relapse following A.C.T.H. therapy in similar cases has been recorded, Ellman (1954) considering it almost invariable in this condition, and it is important to realise the possibility of prolonged, if not indefinite, maintenance treatment being required.

Summary

1. Three cases of prolonged pulmonary eosinophilia are presented.

2. These all occurred among a population of about 150,000 in the course of four years, and in spite of the paucity of published cases in this country it is suggested that the condition is not as uncommon as has been thought.

3. The association of a form of bronchiectasis with many cases of this condition is emphasised and must be considered a factor in prognosis.

4. The response of one case to A.C.T.H. is described.

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ON THE OCCURRENCE OF EOSINOPHILIA IN TUBERCULOSIS TREATED WITH ANTIBIOTICS

A PRELIMINARY OBSERVATION

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The occurrence of side-effects during antibiotic treatment of tuberculosis is now well recognised. These undesirable reactions are most common with para-amino-salicylic acid (P.A.S.), less frequent with streptomycin, and rare with isoniazid in ordinary doses. They occurred in 7, 3 and 1 per cent. respectively of patients receiving each drug (as part of combined therapy) in a recent large survey. (U.S. Public Health Service, 1954.)

The specific action of streptomycin on the eighth cranial nerve was quite soon recognised as a toxic effect. An allergic reaction in the form of skin eruptions with or without fever was recorded as early as 1948, both in patients receiving streptomycin and in their attendants who handled it (Stringfellow, 1948; Crofton, 1953.)

Cuthbert (1954) has described a case of Loeffler's syndrome in a patient receiving streptomycin and P.A.S. for pulmonary tuberculosis.

The toxic effects of isoniazid are few, and are confined largely to the central and peripheral nervous system. No instances of hypersensitivity seem to have been recorded.

P.A.S. has deservedly the most sinister reputation of the three. A number of recent reports have appeared on its toxic manifestations, including one case of fatal allergic reaction (Steininger, Klopfenstein and Woodruff, 1954). Dixon (1954) has reviewed the subject of P.A.S. ' toxicity,' and from the literature has summarised 26 cases of jaundice following its administration. This jaundice was associated with pyrexia and skin rashes and most patients had a considerable eosinophil leucocytosis in their peripheral blood. The author regarded this feature as being of diagnostic importance in the picture of P.A.S. hepatitis. Warring and Howlett (1952), in reviewing the same problem, differentiate " toxic " and " allergic " reactions to P.A.S. Toxic reactions are mostly limited to the gastro-intestinal tract, whilst under the heading of allergy they list acute drug fever and skin rashes, headache, burning eyes, lachrymation and conjunctival injection, transient lymphadenopathy, angioneurotic œdema, anaphylactic shock, spasmodic cough and wheezing, jaundice, granulopenia, and a reaction resembling infectious mononucleosis.

It may be seen that an eosinophilia is associated with many of these hypersensitivity reactions to streptomycin and P.A.S. This paper offers details of a group of patients suffering from tuberculosis and treated by various antibiotic combinations who developed an eosinophilia without any other allergic manifestations.

The possibility of this occurrence was raised during the study of a patient who had a gross overt allergic reaction to both streptomycin and P.A.S.

Mrs. E.S., aged 34, had long-standing pulmonary tuberculosis with more recent apical cavitation. Her leucocyte count was normal. Following four weeks' treatment with streptomycin, 1 gm. twice weekly, and sodium P.A.S., 12 gm. daily, she suddenly developed a temperature of 102° F., loin pain, frequency of micturition, and bleeding *per vaginam*. The cause was not detected and the drugs were continued for a further week, when her temperature had reached 105° F., she was vomiting, her liver and spleen were palpable, and she had developed a rash. This rash proceeded to an exfoliative dermatitis. Her eosinophil count reached 14,000 per c.mm. (+5 per cent. of 31,000 white cells). Cortisone, 350 mgm. over four days, proved dramatic therapy, completely abolishing her symptoms and signs and probably saving her life.

Test doses of streptomycin and P.A.S. showed that she was sensitive to both drugs. She was slowly and uneventfully desensitised to streptomycin and continued on combined therapy with streptomycin and isoniazid to lobectomy two months later. Though she had no recurrence of her allergic symptoms, her eosinophil count remained high, up to 2,500 per c.mm. (35 per cent. of 7,100 white cells). After lobectomy with removal of all radiologically obvious disease, her eosinophil count, as expected, fell to zero in the immediate postoperative period. It then became elevated again but only moderately so (700 to 1,300 per c.mm.). When the drugs were finally suspended her leucocyte count returned to normal.

This chance observation led to a more careful search for an eosinophilia without symptoms in other patients, in the hope of detecting " subclinical allergy " and avoiding similar mishaps. Accordingly, serial leucocyte counts were performed on all patients who remained in hospital for at least one month after commencing treatment (a minority of those given antibiotics). At first, when an eosinophilia was detected, a careful watch was kept for signs or symptoms of allergy, but these failed to appear. We soon realised that we were seeing a number of patients with a symptomless eosinophilia, and that, despite continued antiobiotic treatment, they were remaining quite symptomless, though the eosinophilia persisted.

Over a period of eight months, 36 consecutive patients with tuberculosis who remained in hospital for at least one month have had leucocyte counts performed after commencing treatment with various combinations of streptomycin, P.A.S. and isoniazid. Those patients admitted because of an overt allergic reaction have been omitted. Of these 36 patients, no less than 10 have developed an eosinophil count above normal limits, and none of these has subsequently shown any other allergic manifestations. Details of these 10 patients are given in the accompanying table.

Whitby and Britton (1953) regard 400 eosinophils per c.mm. as the upper limit of normality. Since our figures are not the result of direct eosinophil counts, we have set a rather more stringent standard of 500 per c.mm. Even so, several cases with counts just over this figure have been omitted.

The statement " eosinophilia first seen " is only relative, as some patients may have had the phenomenon for a month or more without having a leucocyte count performed. Similarly, it has not been possible to obtain leucocyte

counts, say six months, after commencing treatment, so that the possibility of a late eosinophil reaction in still more patients cannot be ruled out.

It will be seen that the eosinophilic reaction has occurred in patients on each possible combination of the three antibiotics. Streptomycin is the common factor in all patients, at least for a time, but one patient continued to have a marked eosinophilia on a régime of P.A.S. and isoniazid, months after cessation of streptomycin therapy.

The " course unknown " group represents patients sent to sanatoria, who have had no allergic reactions, but in whom no recent leucocyte counts are available.

The first patient of the table is worth considering in more detail. She was a Polish woman, aged 38, with right upper lobe cavitation and a positive sputum. Her leucocyte count on admission to hospital was within normal limits, and there was no family or personal history or allergy. She was treated on 1 gm.

TABLE I

No.	Disease	Treatment	Eosinophilia first seen	Maximum eosinophil count*	Follow-up without ill-effects	Course of the eosinophilia
1	Pulmonary	SP PH	3 months	3,680 (39)	8 months	Persisted (see text)
2	Pulmonary	SP	2 months	2,300 (19)	6 months	Persisted
3	Pulmonary Laryngeal Intestinal	SPH (D)	1 month	1,265 (11)	1 month	Unknown
4	Pulmonary	SH	1 month	1,100	3 months	Fell, but not to normal
5	Pulmonary	SP	1 month	1,100 (10)	6 months	Fell to normal
6	Pulmonary	SP	6 weeks	1,025 (16)	4 months	Fell, but not to normal
7	Pulmonary	SP	2 months	975 (7)	3 months	Unknown
8	Bronchial	SP	10 weeks	820 (9)	2 months	Unknown
9	Meningitis	SH (D)	2 weeks	1,875 (16)	3 months	Persistent
10	Meningitis	SPH (D)	4 months	640 (9)	3 months	Unknown

S: Streptomycin, 1 gm. twice weekly; or (D) daily.
P: P.A.S. (sodium salt), 12 gm. daily.
H: Isoniazid, 200 mgm. daily; 300 mgm. daily for meningitis.
* The eosinophils are expressed as cells per c.mm. Percentage of total white cells is given in brackets.

of streptomycin twice weekly and 12 gm. of sodium P.A.S. daily, and showed steady improvement. Three months later she was found by chance to have a leucocyte count of 4,600 with 23 per cent. eosinophils. Serial white cell counts showed a persistent marked eosinophilia, with a maximum of 3,680 eosinophils per c.mm. (39 per cent. of 7,900 white cells). After five months she was changed to an isoniazid-P.A.S. combination and the phenomenon persisted. After nine months a segmental resection of her residual disease was performed. Her eosinophil count fell abruptly immediately after operation, as might have been expected. It remained within normal limits for five weeks and then rose again (P.A.S. and isoniazid having been continued throughout).

Comment

Gill (1940), from a perusal of the continental literature, stated that eosinophilia occurs in tuberculosis under the following circumstances:

(a) Following the diagnostic or therapeutic injection of tuberculin. This is known as the Michaelow reaction.

(b) In tuberculous lymphadenitis.

(c) Complicating artificial pneumothorax therapy.

(d) Complicating gold therapy.

(e) Occurring spontaneously in pulmonary tuberculosis.

Nevertheless, eosinophilia arising spontaneously must be exceedingly rare. No patient has been admitted to the beds of this unit in the past year with untreated tuberculosis and an eosinophil leucocytosis. However, eosinophilia in association with other manifestations of allergy to antibiotics has been commonly seen in recent years.

The present report indicates that eosinophilia is quite frequent as an isolated finding in cases of tuberculosis treated with antibiotics; it has occurred in 10 out of 36 unselected patients. The eosinophil count may reach quite high levels, but the higher counts carry on greater risk of overt allergic reactions. These latter reactions occur " out of the blue," and serial white cell counts seem to be of no help in anticipating them.

The high eosinophil count may persist (or even increase) for months, it may fall, or it may return to normal, but, as emphasised, it does not, in our experience, presage true drug sensitivity reactions.

Summary

A well-marked eosinophil leucocytosis developed in 10 out of 36 patients with tuberculosis while under treatment with antibiotics, unaccompanied by any of the associated hypersensitivity reactions recorded in the literature.

Though some of these patients have been followed for six months or more, no allergic symptoms have developed. The eosinophilia is not a danger signal.

It is suggested that the phenomenon will be found to be quite common.

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LETTERER-SIWE'S DISEASE

(REPORT OF A CASE WITH PULMONARY MANIFESTATIONS)

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Letterer-Siwe's disease, so termed after Letterer, who first described the condition in 1924, and Siwe, who described the fourth case in 1933 and reviewed the three previous cases (Schafer, 1949), is classified as a non-lipoid reticulo-endotheliosis.

The " reticulo-endothelial system " first defined by Aschoff, but previously recognised by Metchnikoff, is composed of cells distributed in various areas of the body, which are characterised by their ability to take up particulate matter and to store foreign substances brought to them in colloid solution. These cells are the macrophages of the loose connective tissue, the reticular cells of the lymphatic and myeloid tissues, the von Kupffer cells in the sinuses of the liver, lining cells of the sinuses in the adrenal and the hypophysis, and the adventitial cells about the blood vessels (Maximow and Bloom).

Proliferation of the cells of this system can be caused by infectious and non-infectious conditions. Siwe divided into two categories the diseases of the reticulo-endothelial system not belonging to the then recognised xanthomatoses (Schuller-Christian's, Gaucher's and Niemann-Pick's diseases). In the first group he included those cases associated with an acute infection known as infectious reticulo-endotheliosis; in the second group he placed those cases in which no significant infection was present, now known as Letterer-Siwe's disease. Both are regarded as non-lipoid reticulo-endothelioses (Schafer, 1949).

More recently Leterrer-Siwe's disease, Hand-Schuller-Christian's disease and eosinophilic granuloma have been grouped as associated conditions.

Letterer-Siwe's disease occurs in infancy. Schuller-Christian's disease occurs in early childhood, while eosinophilic granuloma may be found in children and adults.

The etiology of the condition is unknown. An infective basis is postulated by Fisher (1953). McKeown (1954) found features suggestive of neoplasia, while Lumb classifies the condition as a complex abnormality of lipoid metabolism.

Clinically, cases of Letterer-Siwe's disease present as " focal " and generalised proliferation of the cells of the reticulo-endothelial system. Fever, anæmia and constitutional symptoms are generally also present.

Histologically, the " focal " lesions consist of collections of fairly uniform mononuclear cells. Associated with these cells are " giant cells " and eosinophils. The absence of lipoid from the mononuclear cells is the differentiating feature between this condition and Hand-Schuller-Christian's disease.

Case Report

Male infant, aged four months.

The child had originally been seen because of a diffuse skin rash. When first seen by one of us (G.A.B.) because of a right supraorbital swelling, this rash was still present. The right eye was proptosed downward and inward and there was a swelling of the upper lid and excessive lacrymation. A soft tumour was easily palpable inside the upper outer orbit suggesting an enlarged lacrymal gland. The orbital edge was eroded.

Investigation:

> Blood count: R.B.C. 4,140,000; Hb 59 per cent. (8·5 g.).
> C.I. 0·7.
> W.B.C. 4,100: Diff.-Lym. 72 per cent., Mono. 6 per cent.
> Poly. 22 per cent., Eos. 0 per cent., Bas. 0 per cent.
> Urine: N.A.D.

Biochemical investigation was restricted owing to the extreme difficulty in obtaining adequate blood samples.

Symptomatology

The liver and spleen were both enlarged and easily palpable. There were enlarged lymph glands in the axillæ and groins. There was a generalised raised erythematous rash, more marked on the trunk. The only respiratory symptoms noticed were a terminal bronchitis. X-ray of the skull showed a bony erosion deep to the right supraorbital mass. There was prolonged fever ranging from 99° to 105° F., with an occasional apyrexial phase of short duration.

At exploratory operation considerable erosion of the orbital edge and complete destruction of the orbital roof was found. A portion of the mass was taken for examination. Histological examination showed areas of large mononuclear cells with pale cytoplasm. Moderately numerous multinucleated giant cells were present as well as an occasional area showing a few eosinophils (Fig. 1). Dr. C. V. Harrison of the London Postgraduate Medical School, to whom a section was sent, was of the opinion that the histological findings were those of Letterer-Siwe's disease.

A chest film taken in January 1954 (Fig. 2) showed diffuse mottling throughout both lung fields.

Treatment

Penicillin, streptomycin, chloramphenicol, aureomycin, and cremotres-amide were without effect. A total dosage of 400 mgm. of cortisone was given orally. While this effected a remarkable regression of the tumour in the course of a few days, clinically the child continued to deteriorate and the pyrexia was unaffected. The child died in April 1954, aged 11 months. Permission for an autopsy was refused.

Discussion

The radiological appearance of the lungs in this case are of interest because of its rarity. The chest film shows innumerable fine opacities throughout both lungs (Fig. 2). In a few areas these opacities give an appearance of coalescence. Similar radiological findings in the lungs in Letterer-Siwe's disease have been
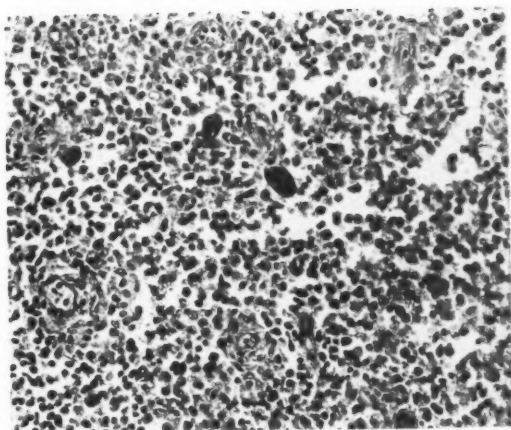
PLATE XI

FIG. 1.—Photomicrograph (X250) showing the general histological features of the orbital tumour.

FIG. 2.—Chest film showing diffuse bilateral mottling.

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described by McKeown. The underlying mechanism of these findings is uncertain. The pathological basis of Letterer-Siwe's disease is a proliferative change in the cells of the reticulo-endothelial system forming "granulomatous" lesions. The possibility that these lesions may themselves account for the radiological appearance and that later degenerative change produce the "honeycomb lung" must be considered. However, McKeown, on the basis of the post-mortem examination of two cases, suggests that "the development of the honeycomb lungs in this condition is no doubt due to bronchial obstruction produced by the dense sheets of histiocytes which surround and infiltrate the bronchial tree. . . ."

To the diseases occurring in infancy giving a radiological picture of diffuse pulmonary mottling, miliary tuberculosis, sarcoidosis and idiopathic pulmonary hæmosiderosis—is added Letterer-Siwe's disease.

Summary

A case of Letterer-Siwe's disease is presented with particular reference to the radiological findings of diffuse miliary mottling in the lungs.

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DYSPHAGIA PNEUMONITIS FOLLOWING EPIDERMOLYSIS BULLOSA

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Epidermolysis bullosa is a rare skin disease, often familial, in which bullæ and subsequently atrophic changes are produced by friction or slight trauma. Lesions are found particularly on the extremities. In the dystrophic variety of the disease they also occur on mucous membranes.

The following case is of interest in that the epidermolysis involved the œsophagus and gave rise to a stricture which in turn led to a "dysphagia pneumonitis."

A housewife aged 32 was first referred to the Chest Clinic by a M.M.R. unit in early 1952, her X-ray having shown opacities in the right lung. Her history as regards chest symptoms was of cough, about two years in duration and most persistent in recumbency. A little mucoid sputum could sometimes be produced. There was nothing in the history to suggest an acute pulmonary episode at any date. Her skin condition had been present since childhood, the main complaint in this respect being of painful or irritating blisters appearing on the limbs in response to any slight trauma. From time to time blisters had occurred in the mouth. She could recall no family history of skin disease. For at least ten years she had had discomfort behind the lower sternum after swallowing. About ten years previously she had attended hospital in a neighbouring town and apparently a " narrowed gullet " had been confirmed by œsophagoscopy. Attempts at dilatation of the œsophagus had been unsuccessful. There was no vomiting after food, but a little regurgitation sometimes occurred.

The patient when first examined was a thin woman appearing older than her years. Weight was 95 lb., her best weight being 100 lb. Hair was grey and sparse and there was a generalised deficiency of subcutaneous fat. Skin, but not mucosæ, was pale generally.

The skin of feet and hands was smooth and shiny and thickened, that over the dorsal surfaces of hands and fingers being hyperæmic and blue. Over pressure points on the limbs and over areas of previous trauma were scaly red scarred patches. A few tender vesicles with raised injected margins were present, located on the dorsal surfaces of hands and fingers, ankles and shins. Nails were all absent.

Examination of the respiratory system revealed medium inspiratory rhonchi throughout the right chest. The larynx was normal. No abnormality was found on examination of the central nervous or cardiovascular systems or abdomen.

Investigations. Sputa: (3) negative for acid-fast bacilli on direct examination and culture. Urine: no sugar, albumen or deposit. B.S.R. (Wintrobe, cor-

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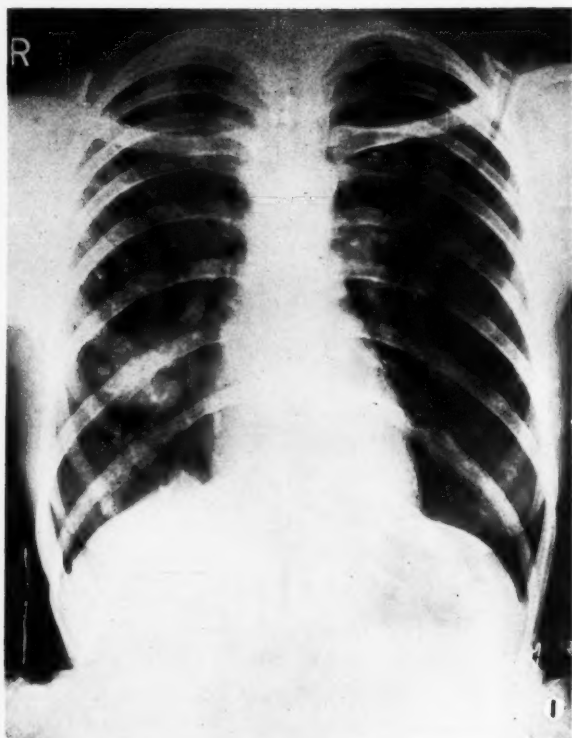re
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PLATE XII

FIG. 1.—Right lung shows mid-zone infiltration and fibrosis typical of " dysphagia pneumonitis."
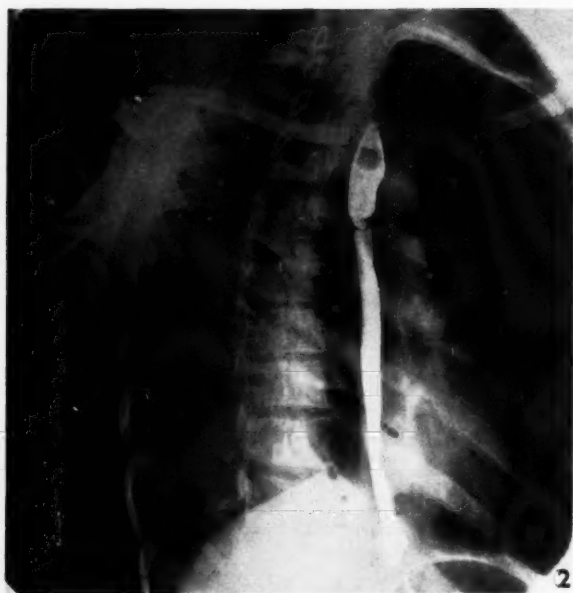

FIG. 2.—Barium swallow demonstrates stricture at junction of upper third and lower two-thirds of œsophagus.

rected): 26 mm. in one hour. Blood count: Hb. 82 per cent. R.B.C. 4,210,000 (normal erythrocytes), C.I. 0·97, W.B.C. 9,200, polymorph neutrophils 53 per cent., lymphocytes 45 per cent., monocytes 2 per cent.

Chest X-ray (Fig. 1). In the right lung were visible a soft irregular opacity in the mid-zone and two smaller similar opacities below the clavicle. Scattered mottling was also seen and striated areas suggesting fibrosis. The inner third of the diaphragm was tented. The left lung appeared normal.

X-ray screening. The diaphragms both appeared sluggish in movement, but there was no paralysis.

Barium swallow (Fig. 2). A stricture was demonstrated just below the curved impression of the aortic arch. The radiological appearance of the stricture was reminiscent of the description of œsophageal strictures arising from peptic ulceration (Cochrane Shanks, 1951). There was a regularity and smoothness about the channel which did not suggest malignancy. The lumen was central, the walls were parallel and the entrance to the stricture was well defined. The site of the stricture was at the junction of the upper third and lower two-thirds of the œsophagus, where striated muscle changes to smooth muscle.

The patient was later referred to Dr. I. Sneddon, Consultant Dermatologist, who gave the diagnosis of epidermolysis bullosa, variety dystrophica.

In the ensuing two years the patient has been seen at intervals. There has been little change in her symptoms and physical findings, but the occurrence of several fresh telangiectatic lesions on the pharyngeal wall has now added to the difficulties of swallowing. The chest X-rays show a little clearing of the right lung opacities. The striated markings of fibrosis are rather more evident, but there is no obvious mediastinal retraction.

Discussion

A report of the findings at œsophagoscopy unfortunately were not available in this case, but the long-standing stricture is no doubt a sequel to involvement of the œsophageal mucosa by the lesions of the epidermolysis bullosa.

Among thirty-seven cases of this disease having mucous membrane involvement, collected from the literature by Tobias (1928), two cases had œsophageal lesions.

The present patient was unwilling to have further œsophageal investigation. Indeed, as there seems adequate evidence without this to establish the diagnosis, the trauma of endoscopy would be better avoided. Œsophagoscopy was carried out in one of the cases described by Tobias, and following this operation numerous hæmorrhagic bullæ and erosions in the upper third of the œsophagus appeared.

The pulmonary conditions resulting from stricture of the œsophagus or achalasia have been fully described by Belcher (1948). Repeated small spills into the bronchial tree may lead to such complications as lung abscess, collapse, lung fibrosis, or a non-specific inflammation of the interstitial tissue of the lung. The last mentioned is often referred to as " dysphagia pneumonitis," and is the condition indicated by the history and X-ray appearances in the present case.

It is interesting to note that the cough of this patient was aggravated by recumbency, as it is considered that spills into the bronchial tree occur mainly in that position, especially during sleep, when the cough reflex is diminished.

Summary

A case of dysphagia pneumonitis is described. The cause of the pulmonary condition was repeated spills into the bronchial tree as a consequence of an œsophageal stricture. The stricture was due to epidermolysis bullosa.

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AN UNUSUAL CASE OF BRONCHIAL ADENOMA

By J. H. P. Johnson

From The East Ham Chest Clinic, London

COMBINED lesions often provide a fascinating problem in diagnosis and treatment and the following case is an illustration. Underlying causes for the presenting feature or the chance association of a second lesion are usually missed because they are not suspected or sought, or because the correct significance is not attached to unusual or unexpected aspects of the case or to relevant points in the history.

Case Report

A woman aged 32 years was referred to Dr. Philip Ellman at East Ham Chest Clinic in October 1952, complaining of persistent cough, lassitude and breathlessness on exertion which had persisted since the onset of her illness in 1947. Her history was as follows:

She was well till February 1947, when she developed a right pleural effusion with intermittent pyrexia and a productive cough. She rested at home for two months, but then had an exacerbation of her symptoms and was admitted to a general hospital on 5.4.47. X-ray of her chest confirmed the presence of a large effusion and also showed collapse of her right lower lobe, but this does not seem to have been appreciated at the time. She was treated initially by repeated aspirations and instillation of penicillin, together with penicillin parenterally, but as the fluid, which was at first thin and purulent, became thick and chocolate-coloured, surgical drainage was carried out on 18.4.47; culture of the pus revealed *H. influenzæ* only. She made a good recovery from the operation and was followed up as an out-patient till 1949. Serial X-rays of her chest during this period showed some mottling in the right upper zone which gradually spread during the next few months into the right middle and left upper zones; there was also a persistent opacity at the right base due to a residual empyema and the collapsed lower lobe. In 1948 she developed tuberculous arthritis of her right knee and, a little later, lupus vulgaris. In 1949 she had a large hæmoptysis but apparently did not receive any specific treatment. The sinus in her chest following her operation remained open and continued to discharge a thin purulent exudate right up to the time she attended the Chest Clinic in October 1952.

On examination her general condition was good and she had, in fact, gained 2 stone in weight in the previous five years; there was no finger clubbing. Examination of her chest showed the trachea to be deviated to the right; there were persistent crepitations at the right upper zone and dullness to percussion, absent breath sounds at the right base, and a sinus with a thin purulent discharge. X-ray examination of her chest showed infiltration in both upper zones and in the right middle zone with a cavity in the right apex, which was later confirmed on tomography; the right lower lobe was collapsed, there

was pleural thickening at the base and an encysted empyema which was shown to be in the paravertebral gutter on tomograms (Figs. 1 and 2). X-ray of her right knee showed a tuberculous lesion. Her sputum was positive for tubercle bacilli, her E.S.R. was 58 and pus from the sinus was sterile on culture. A pleurogram confirmed the presence of the empyema space but did not reveal its extent.

She was referred to Mr. Geoffrey Flavell at the London Hospital and was admitted there on 6.2.53. Bronchoscopy on 11.2.53 showed the right stem bronchus to be totally occluded by a smooth lobulated mass at the level of the right upper lobe bronchus which just aerated above it. Biopsy showed acid-fast bacilli in granulation tissue, but further biopsy revealed, in addition, the presence of an adenoma.

Treatment was started with Streptomycin 1 gm. intramuscularly, twice weekly, with Isoniazid 100 mg. three times daily by mouth, and this was continued till after the operation. On 7.4.53 a right pleuropneumonectomy was carried out, followed on 29.4.53 by a right thoracoplasty. She made a good recovery and subsequently spent four months convalescing at Broomfield Hospital. Since being discharged she has remained in good health and free from symptoms, the sinus has remained closed and her sputum has been persistently negative.

The specimen removed at operation showed tuberculous infiltration throughout the right lung, with cavitation in the right upper lobe. A large adenoma almost completely occluded the right stem bronchus and was encroaching on the main divisions. The right lower lobe was shrunken and the bronchi were grossly dilated and infected; the pleura was thick and enclosed a loculated empyema (Fig. 3).

Discussion

There can be little doubt that the adenoma had been present at the onset of her illness and bronchoscopy, which should have been done, would have revealed it. The persistence of the discharging sinus for so long indicated the presence of a chronic empyema and should have suggested a closer assessment of the condition of the underlying lung and of the bronchi. The hæmoptysis in 1949 was an additional clue to the true diagnosis, but presumably was dismissed as being of little significance and no further investigation was done. It is probable that the bleeding was attributed to the pulmonary tuberculosis which may not have seemed to merit treatment, as she was not rested and no record could be found of any positive sputa, nor whether her sputum had been examined at that stage. There was enough indication, however, that her tuberculous disease was active as it had spread in her lungs and she developed tuberculous arthritis of her right knee and lupus vulgaris at about the same time. It is remarkable that her general condition remained good and she gained 2 stone in weight, and that her fingers were not clubbed.

At the time she attended the Clinic, pleuropneumonectomy was the ideal treatment and served to remove the adenoma, the cavitated and non-cavitated tuberculous lesions in the right lung, the collapsed and bronchiectatic lower lobe and the diseased pleura and empyema space at one operation. It was fortunate that the tuberculous lesions in the left lung were quiescent and allowed this to be done.

PLATE XIII

FIG. 1.—Postero-anterior radiograph showing mottling in all zones of the right lung and in the left upper zone. The right lower lobe is collapsed and there is a dense opacity at the base extending into the paravertebral region due to the encysted empyema.

FIG. 2.—Right lateral radiograph showing the collapsed right lower lobe and the basal pleural involvement.

FIG. 3.—Photograph of the specimen removed in operation showing a large adenoma filling the main bronchus and extending into the basal branches, which are grossly bronchiectatic. There is a good deal of surrounding fibrosis and the pleura is thickened.
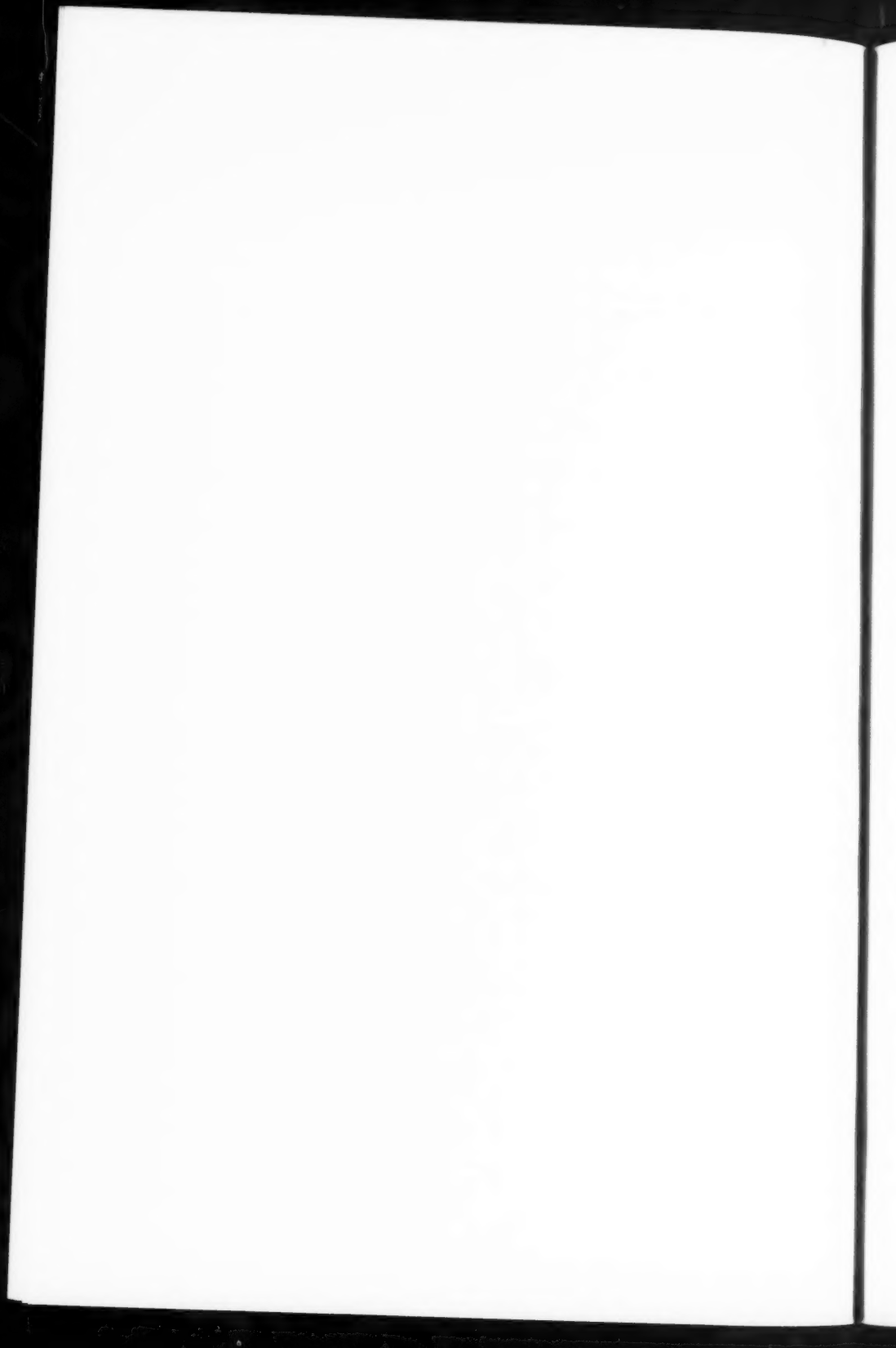
Summary

A case is described of a woman aged 32, in whom a chronic empyema occurred secondary to a bronchial adenoma which went undiscovered for five years. In the interval pulmonary tuberculosis occurred and led to cavitation in the upper lobe of the same lung and ultimately pleuropneumonectomy followed by thoracoplasty led to complete recovery.

REVIEWS OF BOOKS

Tuberculoma of the Lung. By OLLE HILLERDAL. Copenhagen: Ejnar Munksgaard. 1954. Supplement 34 to Acta Tuberculosea. Pp. 190. Illus. Price 45s.

This is an excellent monograph, but dull. It is based on a painstaking study of the serial radiographs of nearly 35,000 persons who attended the lung clinic of the University of Uppsala during fifteen years. Two hundred and one showed rounded, sharply defined opacities, at least 1 cm. in diameter. More than half the book is made by the case histories of these patients, many of which are illustrated by satisfactory reproductions of radiographs. A few of the shadows were caused by neoplasms, cysts or abscesses, but the majority were due to proved or suspected tuberculosis. Various degrees of certainty of diagnosis are classified, to the confusion of the reader but no doubt to his scientific satisfaction. The groups so formed are analysed as to various features of interest in detail, with many tables. As the follow-up is complete, and in more than three-quarters of the patients has been for over three years, the conclusions are authoritative. While the cautious discussion of radiological features, symptoms, pathogenesis and diagnosis is of some interest, no new facts are disclosed and most readers will be more concerned with the course of these lesions, and perhaps sometimes surprised at its benignity. Spread was unusual and easily controlled: in most cases regression occurred. The natural history has inevitably been modified by treatment in two-thirds of the cases, by methods too varied to subject to statistical analysis. It is unfortunate that the course in those not treated has not been analysed separately.

The definition of tuberculoma accepted is a radiological one; cavitation is not excluded. Separation from other forms of tuberculosis is easy, but as at least three different pathogeneses are possible, and as an arbitrary size of lesion is accepted, no fundamental differences must be supposed to exist and the classification is for practical convenience only.

Dr. Hillerdal's conclusions will be accepted by most clinicians. He advises that operation should be performed when there is doubt as to diagnosis, and that in other cases observation alone is necessary unless there are signs of activity, when sanatorium care and chemotherapy are indicated. Not all will agree that artificial pneumothorax plays a part, and his sound advice that resection when performed should be as conservative as possible must be tempered by our knowledge of the frequency of adjacent satellite lesions.

The monograph begins with a somewhat conclusive review of the literature. (There are ten pages of reference.) The whole work will only be read by those who are themselves writing a thesis or an article, but the conclusions presented in the last seven pages are of great interest to all who deal with lung disease. It has been translated into faultless English by Dr. Bergman, and is well produced.

M. MEREDITH BROWN.

The Surgery of Pulmonary Tuberculosis. By JAMES H. FORSEE. London: Henry Kimpton. 1954. Pp. 208. 59 Illus. 48s.

This short book (203 pages) is one of the best accounts of the surgery of pulmonary tuberculosis recently published, and accurately reflects the modern

trend towards greater employment of resection as opposed to collapse therapy and especially to segmental excisions conserving the maximum of healthy lung —although the point is well made that " healthy " in this context is a strictly relative term.

Col. Forsee prefaces his monograph by claiming that 91 per cent. of patients treated in the past seven years at his Army Hospital by pulmonary excision are well and working, and this happy transformation in prognosis can certainly be confirmed here, although it is clear his patients fall largely in the younger age groups.

He has completely abandoned the use of plastic plombages, currently fashionable in England, because of their bad conversion record, preferring thoracoplasty, which he performs under general anæsthesia, omitting, one is sorry to see, any attempt at apicolysis: surely retrogressive steps. In the detailed account of surgical techniques surgeons of course differ; but it is surprising to read " the surgeon with accurate knowledge of the anatomy of the pulmonary hilus will regularly require three to four hours in the performance of lobectomy." Life for Col. Forsee must be long indeed.

The X-ray reproductions are, as is so often the case, not very good: and perhaps this is why one doubts the success of the adhesion cutting depicted in Fig. 22 (c). On the whole I think the book helpful, clear and honest; even if it is spattered from beginning to end with split infinitives.

Anatomy of the Bronchovascular System, its Application to Surgery. By GEORGE L. BIRNBAUM. Chicago: The Year Book Publications. 1954. (Distributed in Great Britain by Interscience Publishers Ltd.) Pp. xv+299. Illus. 112s.

As an occasional sport or odd mutation is taken in the stride of highly prolific families, so this work could have dropped only from the busy rollers of American science publications. It consists almost wholly of quotations from such a profusion of other writers that the effect on this reviewer is one of well-documented confusion; nor has much attempt been made to evaluate the relative worth of the opinions recorded.

The first third of the book is an account of bronchovascular anatomy and its variations, whose percentage incidence is given in numerous tables, sometimes to two places of decimals. Unfortunately international nomenclature has not been adhered to; and a curious algebraic notation of great complexity is subsequently used in referring to the various bronchial and vascular branches. The remainder of the volume is devoted to a more or less detailed account of the surgery of vascular anomalies, animal experimental surgery, and pulmonary resection. A disproportionate amount of space is occupied by two sections on the surgery of asthma.

Expensively produced, richly but unsatisfactorily illustrated, to whom, one wonders, is this work addressed?

GEOFFREY FLAVELL.

Technique and Results of Fluoroscopy of the Chest. By E. A. ZIMMER (trs. E. W. Loos). Illinois: Charles C. Thomas (Published British Commonwealth: Blackwell Scientific Publications), 1954. Pp. xiv+135. 40s.

This book is an attempt to describe the art of chest fluoroscopy. The chapters dealing with the nature and production of X-rays, protection, dark

adaptation and the technique of screening are good; but the larger part of the book concerned with the results is less successful.

The author places too much emphasis on diagnosis—surely there is little point in attempting to distinguish on the screen between silicosis and sarcoid? Not enough space is given to conditions which are best investigated by fluoroscopy, such as obstructive emphysema and eventration.

The section on the heart is poor: valvular calcification is barely mentioned and hilar pulsation and the alteration in the lung field vascularity in congenital heart disease is not discussed.

This is only a slim volume, but it could with advantage be even slimmer, as many of the author's explanations are improbable, though his observations may be correct. The book is a translation from the German which has been rearranged in America; the result is often long-winded and sometimes difficult to understand.

JOHN PIERCE.

The Scalpel, The Sword. The Story of Dr. Norman Bethune. By SIDNEY GORDON and TED ALLEN. London: Robert Hale Ltd, 1954. Pp. 271. Price 16s.

Dr. Norman Bethune was a stimulating if at times unstable personality and there is no doubt that his biography is a stimulating and enthralling book. He was a man who dedicated himself unreservedly to the cause of the moment, whether it was artificial pneumothorax, thoracic surgery, the Spanish Civil War or the Sino-Japanese war, and his pioneering work in field surgery anticipated such work in the second World War. He was a man of tremendous personal courage, but one feels that he increased the odds against himself by his inability to delegate authority. Those who were closest to him became imbued with his own selflessness, but one feels there were many who were antagonised by his ruthlessness, and had he been a little more unstinting in what he gave of himself the world would not have been the poorer by the untimely death of one who was, from many points of view, a saint.

Dr. Bethune became successively a socialist and a communist. It requires little imagination to realise how many of his Canadian colleagues he would alienate in this evolution during the 1930s. History has not yet pronounced a final verdict on his opinions, but the reader of this book cannot fail to be enlisted on the side of those whom he fought to succour. As a clinician he has perhaps been superseded, but in his versatility—he was painter, sculptor and author as well as a doctor—he embodied the highest qualities of the medical profession, recognising the spiritual ills of man no less than his physical ones.

" The Scalpel, The Sword," is not primarily for the medical reader—some doctors may find in Bethune's life an inspiration, but all will find in it the portrait of a dynamic and, for all his faults, a magnificent personality.

The Brompton Hospital. The Story of a Great Adventure. By MAURICE DAVIDSON and F. G. ROUVRAY. London: Lloyd-Luke (Medical Books), 1954. Pp. 152. 21s.

Although The Royal Chest Hospital was founded some years before the Brompton Hospital, the latter has for many years been synonymous with diseases of the chest, to lay as well as to medical men. It is difficult for this generation to realise that in 1840 the doors of hospitals were closed to victims of tuberculosis, which was then a far greater and more widespread scourge than it is today. Sir Philip Rose, the founder of the Brompton, has been a

benefactor to countless thousands, and to his humanity and far-sightedness the authors of this book pay due and just tribute.

As a survey of a hundred years' work the volume is a masterpiece of compression and lucidity, and in Dr. Davidson's inimitable style remains essentially readable. It is an absorbing story that the authors have to tell and a satisfying one, for the century was one of achievement. The men who pioneered and fostered the Brompton Hospital may well contemplate with pride their work.

The book is beautifully printed and presented, with photographs of historical and personal interest that are not merely decorative adjuncts to the volume but are intrinsic to it. The volume lives up to the high standard that is always expected and received from the Brompton Hospital.

PHILIP ELLMAN.

Traitement de la Tuberculose Pulmonaire. By JEAN PARAF, PIERRE ZIVY, and MADELEINE PARAF. Paris: Masson and Cie. 1954. Pp. 212. 3 Figs. Price 950 fr.

This is an up-to-date discussion on the treatment of pulmonary tuberculosis, with particular reference to the changes which have occurred during recent years as a result of the development of specific chemotherapy.

The first chapter, on diagnosis, is well worth reading, for it is upon the premise of early diagnosis that the whole structure of successful treatment is founded. The authors stress the necessity for giving adequate time to obtaining a complete history and also to carrying out a thorough physical examination, even though they agree that physical signs are absent in more than 60 per cent. of cases of active tuberculosis. They very properly lay stress upon the necessity for an X-ray examination of the chest in every patient who has any type of respiratory symptoms for more than fifteen days, and they go so far as to state that omission to carry out this examination in such circumstances is a serious professional default.

The section of rest contains a discussion on the advantages and disadvantages of residence in a sanatorium, as compared with rest at home, from which it would appear that domiciliary treatment in France occupies much the same place as it does in this country. Chemotherapy is used extensively, and the section on P.A.S. is interesting in that it stresses the advantages of giving this substance by an intravenous drip. The technique is fully discussed.

The authors have a good word for artificial pneumothorax, which they still regard as being a most valuable method of treatment, and they devote a lengthy chapter to all its relevant aspects. Pneumoperitoneum is more briefly discussed, and with less enthusiasm.

The surgery of pulmonary tuberculosis is considered at length, in a tabular form which is easy to follow. If treatment is to consist primarily in attention to anatomical changes, then this table is useful, but tabulation seems to detract from the individual and personal nature of the problem of surgery as applied to patients, each of whom differs in personality and in prospect of response to a major operation.

The final chapter briefly discusses tuberculosis in relation to the community. France has a social security system and the rules and regulations are set out here. It would appear that, as in the country, there is adequate provision for the sick patient and that the factor of financial worry incidental to the illness is considerably reduced.

JAMES MAXWELL.

Lehrbuch der Tuberkulose des Kindes und des Jugendlichen. By W. CATEL. Stuttgart: Georg Thieme Verlag. 1954. Pp. xvi+550. 142 Illus. D.M. 59.40.

This book presents a detailed description of the general pathology of tuberculosis with reference to tuberculosis in children and adolescents. It bears the character of a reference book rather than that of a textbook. A stupendous number of facts and literature are presented, which will be useful to specialists in the field of tuberculosis.

Klinisch-röntgenologische Differentialdiagnostik der Lungenkrankheiten. By LASAR DUNNER. Stuttgart: Ferdinand Enke Verlag. 1954. Pp. xi+274. 318 Illus. Price D.M. 49.

A book on the differential diagnosis of pulmonary diseases, both from a clinical and radiological point of view, is a bold undertaking and the author recognises its difficulty. He confesses in his preface that a book on differential diagnosis may be written in various ways and that the individual reviewer might miss some descriptions or consider others unnecessary.

It is not proposed to review the book in a hypercritical frame of mind. Knowing full well the difficulties of differential diagnosis in chest diseases, I think that the author has done well. The usefulness of his book is limited by the fact that the author relies almost entirely on his own experience, and also by the neglect of the fundamentals of clinical and radiological observation— notably the normal anatomy of the chest and its X-ray picture, the pathogenesis and morbid anatomy of pulmonary diseases, etc. It is doubtful whether the reader of the book will be aware of the basic facts indispensable to the interpretation of clinical and radiological symptoms and signs. The omission of tomograms is probably due to some deficiency in the author's technical equipment.

The book will chiefly interest chest specialists, but it is doubtful if they will always agree with the author's interpretation of his X-ray pictures.

Das transversale Schichtverfahren. By A. GEBAUER and A. SCHANEN. Stuttgart: George Thieme Verlag. 1954. Pp. 313. 469 Illus. D.M. 97.50.

This book dealing with tomography, and especially with transverse tomography, does credit both to the authors and publishers. Where it is not possible to obtain good stereoscopic X-ray pictures of the chest, tomography is indispensable in many cases. The authors have now added transverse to routine vertical tomography. They deal thoroughly with the technique and the results obtained from this method. Many cases are analysed and illustrated. The authors have advisedly based their method on anatomy and on the lucid interpretation of their films. The analysis of skiagrams from an anatomical point of view is so often neglected that the constant reference to anatomy in this work considerably enhances the value of the book.

The technique of transverse tomography is not simple nor is the interpretation of the films, as the authors point out themselves in their preface. A disadvantage of the method, apparent in the illustrations, is that it seems difficult to obtain clear-cut outlines in transverse tomograms.

It is likely that the book will owe much of its success to the production, for the publishers, well known for their admirable production, have excelled themselves in this volume.

The book is a valuable addition to the application of radiological diagnostic methods and can be recommended to all engaged in X-ray diagnosis.

S. ENGEL.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in the subsequent issues:

Pulmonary Diseases. Edited by Roscoe L. Pullen. London: Henry Kimpton, 1955. Pp. 669. 195 Illus. 4 Plates. £5 10s.

The Health Visitor and Tuberculosis. By Sheena H. Buchanan. London: The National Association for the Prevention of Tuberculosis, 1955. Pp. 150. 8s. 6d.

Health Horizon. Winter 1955. N.A.P.T. Pp. 56 with Illus. Quarterly. 2s. 6d.

Biochemical Determinants of Microbial Diseases. By René J. Dubos. Harvard: University Press (London: Geoffrey Cumberlege). 1955. Pp. viii+152. 28s.

County Council of the West Riding of Yorkshire: Annual Reports of the County Medical Officer and the Principal School Medical Officer for the year 1953. Pp. 127.

A Study in Spinal Tuberculosis in Childhood. With special reference to some Medico-Social and Clinical aspects. By Lars Mårtenson (trs. L. James Brown). Acta Tuberculosea Scandinavica, Supplement XXXVII (37). Copenhagen: Ejnar Munksgaard, 1954. Pp. 144.

Studies on the Inter-Relationship of Hyperlipemia-Hyperproteinemia and Amyloidosis-Arteriosclerosis. By Gustaf-Adolf Johansson. Acta Tuberculosea Scandinavica, Supplement 35. Copenhagen: Ejnar Munksgaard. 1954. Pp. 69. Illus.

Initial Tuberculous Pleuritis in the Finnish Armed Forces in 1939-1945. With Special Reference to Eventual Postpleuritic Tuberculosis. By Jorma Pätiälä. Acta Tuberculosea Scandinavica, Supplement XXXVI. Copenhagen: Ejnar Munksgaard. 1954. Pp. 57.

Patho-Physiologie der Atmung in der Lungenchirurgie. By J. Maurath. Stuttgart: Georg Thieme Verlag. 1955. Pp. 80. 21 Illus. D.M. 19.50.

Die Grundlagen der Transplantation von fremdem Knochengewebe. By W. Lentz. Stuttgart: Georg Thieme Verlag. 1955. Pp. viii+111. 69 Illus. D.M. 18.

Die Bronchographie. By Ernst Stutz and Heinz Vieten. Stuttgart: Georg Thieme Verlag. 1955. Pp. viii+250. 181 Illus. D.M. 59.40.

Die Cytologie des Bronchialsekretes. By P. Partmann. Stuttgart: Georg Thieme Verlag. 1955. Pp. viii+112. 68 Illus. D.M. 24.

REPORTS

THE THORACIC SOCIETY

THE Spring Meeting of the Thoracic Society was held on March 4 and 5, 1955, at the Royal College of Surgeons. There was a Symposium on " Fungous Diseases of the Lungs " and " Virus Diseases." Other subjects discussed were: " The Prognosis of Bronchiectasis and the Results of a Follow-up "; " Segmental Resection for Bronchiectasis "; and there were short communications on: " The Value of Tomography in Bronchography," by Dr. T. M. Wilson; " A Controlled Trial of Hexamethonium Bromide in Severe Emphysema," by Dr. K. Dormandy; " Differential Comparison of Lung Function by Regional Air-Sampling," by Dr. G. H. Armitage; and " Lymph Node Dissections on Specimens of Lungs or Lobes removed by Operation for Carcinoma of the Bronchus," by Mr. H. C. Nohl.

The Summer Meeting of the Society will be held in Cambridge on July 1 and 2.

ANNUAL REPORT OF THE MEDICAL OFFICER OF HEALTH, CITY OF GLASGOW, 1953

DR. STUART LAIDLAW, in a preface to his Annual Report, makes the following observations on tuberculosis:

" The position regarding tuberculosis has in late years tended to evoke some expressions of doubt or even of alarm, and certainly the continued high incidence of pulmonary disease cannot be regarded as other than serious. While it is still essential to take every step to improve a situation which remains unsatisfactory, there are favourable indications which also deserve some emphasis.

Further improvements have been recorded in the quality and purity of the milk supply. No sample of milk delivered to the schools has been found to contain tubercle bacilli for the past nineteen years.

It is disappointing to have to record a higher incidence of pulmonary tuberculosis in 1953, as shown by an increase of 104 notified cases compared with 1952. It would be a mistake, however, to place a hasty interpretation on this in view of the ever-increasing efforts being made both by the hospital authorities and by the Department to find new cases. As noted elsewhere, for example, the X-ray Unit attached to the Department, which deals with particularly vulnerable groups, completed its first full year of operation in 1953, during which over 200 cases of apparently active lung disease were detected out of 10,500 examinations made. As many of these were registered as new cases, there is good evidence that the increase in notifications is largely, if not wholly, due to more intensive efforts in case-detection. Moreover, the search is being conducted more extensively in groups not previously included in the anti-tuberculosis programme.

While the incidence of pulmonary tuberculosis remains a major problem, the death rate shows another substantial drop, having fallen by one-half in only three years. The non-pulmonary death rate shows an even more spectacular drop of two-thirds in the same period and its incidence also continues downwards.

Another favourable aspect which seems to deserve some emphasis is that the small decline in non-pulmonary tuberculosis conceals a greater decline in the recorded cases of disseminated tuberculosis, which very largely consist of tuberculous meningitis. Moreover, for the first time on record, there was in 1953 no notified case of tuberculous meningitis under the age of one. Indeed, if this is at all an accurate reflex of the true position, it may be fittingly described as a milestone of achievement. It may be that cases of tuberculous meningitis did occur among infants in 1953; but if so they were not formally notified. It seems desirable to emphasise that notification is important and that there is still an obligation on all practitioners to notify cases of tuberculosis forthwith to the Medical Officer of Health. In brief, it should be regarded in the same light as any other infectious disease.

The rapid expansion of B.C.G. vaccination continues, and constitutes yet another heartening aspect of the problem. The success of the new scheme initiated in 1953 for school children should not obscure the fact that progress was well maintained both among contacts and also new-born infants. Indeed, it is tempting to believe that B.C.G. vaccination may have had a decisive influence in the trend of tuberculous meningitis noted. Whether or not this deduction is warranted, there is some cause for believing that the position of tuberculosis as a whole is not one that justifies an attitude of unrelieved despondency."

NOTES AND NOTICES

SOUTH-WEST METROPOLITAN REGION CHEST DISEASES GROUP (EASTERN AREA)

THIS Group has been formed as an independent clinical body, covering the county areas of Surrey and West Sussex, and that portion of the County of London within the geographical area of the Regional Board. The aims and objects of the Group are to promote the study of diseases of the chest, with special reference to the problem of tuberculosis. The Officers of the Group are as follows:

Dr. W. J. Gill (President), Sir Geoffrey Todd (Vice-President), Dr. R. H. J. Fanthorpe (Chairman), Dr. P. C. Anderson, Dr. H. F. Harwood, Dr. J. V. Hurford, Dr. L. J. Rowley, Dr. J. E. Wallace, Dr. F. J. H. Walters (Hon. Treasurer), Dr. G. C. Taylor (Hon. Secretary, 27, Queen Anne Street, London, W.1) from whom full particulars of membership can be obtained.

The first clinical meeting of the Group will be held at St. James' Hospital, Ouseley Road, Balham, London, S.W.12, on Saturday, April 23, 1955, at 2.30 p.m., when the guest speaker will be Sir Clement Price Thomas.

ASIAN AND PACIFIC TUBERCULOSIS CONFERENCE
TO BE HELD IN AUSTRALIA

THE first International Tuberculosis Conference to be held in Australia will take place in Sydney, with the support of the Commonwealth Government, in the week commencing August 15, 1955, immediately preceding the Australasian Medical Congress of the British Medical Association.

The " Colombo Plan " countries will be represented as well as representatives from the World Health Organisation, islands and dependencies in the Pacific area controlled by the South Pacific Commission and voluntary organisations in New Zealand, Singapore, Fiji and elsewhere. Invitations have been sent to the National Association for the Prevention of Tuberculosis, the National Tuberculosis Association of U.S.A. and the Canadian Tuberculosis Association. It is anticipated that many delegates from all Australian States and New Zealand will attend.

After the opening ceremony, which will take place in the Great Hall of the Sydney University, Scientific and Clinical Meetings will be held at the University and at various teaching hospitals in the city of Sydney over the succeeding four days. Visits will also be paid to sanatoria. The main theme of the Conference will be the prevention of tuberculosis and will feature the part played by all members of the medical team whether they be doctors, nurses or social workers. Details of the Conference will be gladly forwarded upon request to the Honorary Director, N.A.P.T.A., Box 852, G.P.O., Sydney, N.S.W.